# Chemioembolizzazione endovascolare

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# Definizione e standardizzazione della terminologia

- **Ablazione tumorale:** ***diretta*** **applicazione di agenti chimici o fisici ad uno specifico sito tumorale nel tentativo di ottenere una distruzione tumorale completa o sostanziale**
- **Procedure endovascolari:** ***indiretta*** **applicazione di agenti chimici o fisici attraverso l'albero vascolare ad un organo sede di tumore a scopo citoriduttivo**
- **Procedure miste: associazione tra le due per potenziare l'effetto**

Gan To Kagaku Ryoho. 2009 Nov;36(12):2318-20.

## [A long-term survival case of liver metastasis of gastric cancer under interdisciplinary therapy].

[Article in Japanese]

Igarashi Y, Aoki T, Kobayashi K, Tanizaki K, Yamanaka C, Komori T, Matsumoto T, Takachi K, Nishioka K, Uemura Y.

Department of Surgery, Kinki Central Hospital of Mutual Aid Association of Public School Teachers.

### Abstract

We report herein a long-term survival case of liver metastasis after distal gastrectomy for gastric cancer. A 72-year-old woman, whom we performed distal gastrectomy with D2 lymph node dissection for type 2 gastric cancer at age 66, was diagnosed as pT2N1M0, stage II. No adjuvant therapy was performed. Liver metastasis was found 1 year and 7 months after surgery. PTX plus CPT-11 was performed. Six courses of therapy were done, and found cCR in the liver metastasis. A total of 23 courses of therapy were done. A recurrence of liver metastasis was found, transcatheter arterial chemoembolization (TACE), radiofrequency ablation( RFA)and operation were performed. She received S-1 plus CDDP, and cCR has been maintained for 6 years and 11 months after gastrectomy (5 years and 4 months after liver metastasis) suggesting that the interdisciplinary therapy was effective.

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J Med Case Reports. 2011 Aug 25;5(1):416. [Epub ahead of print]

## Multi-modality curative treatment of salivary gland cancer liver metastases with drug-eluting bead chemoembolization, radiofrequency ablation, and surgical resection: a case report.

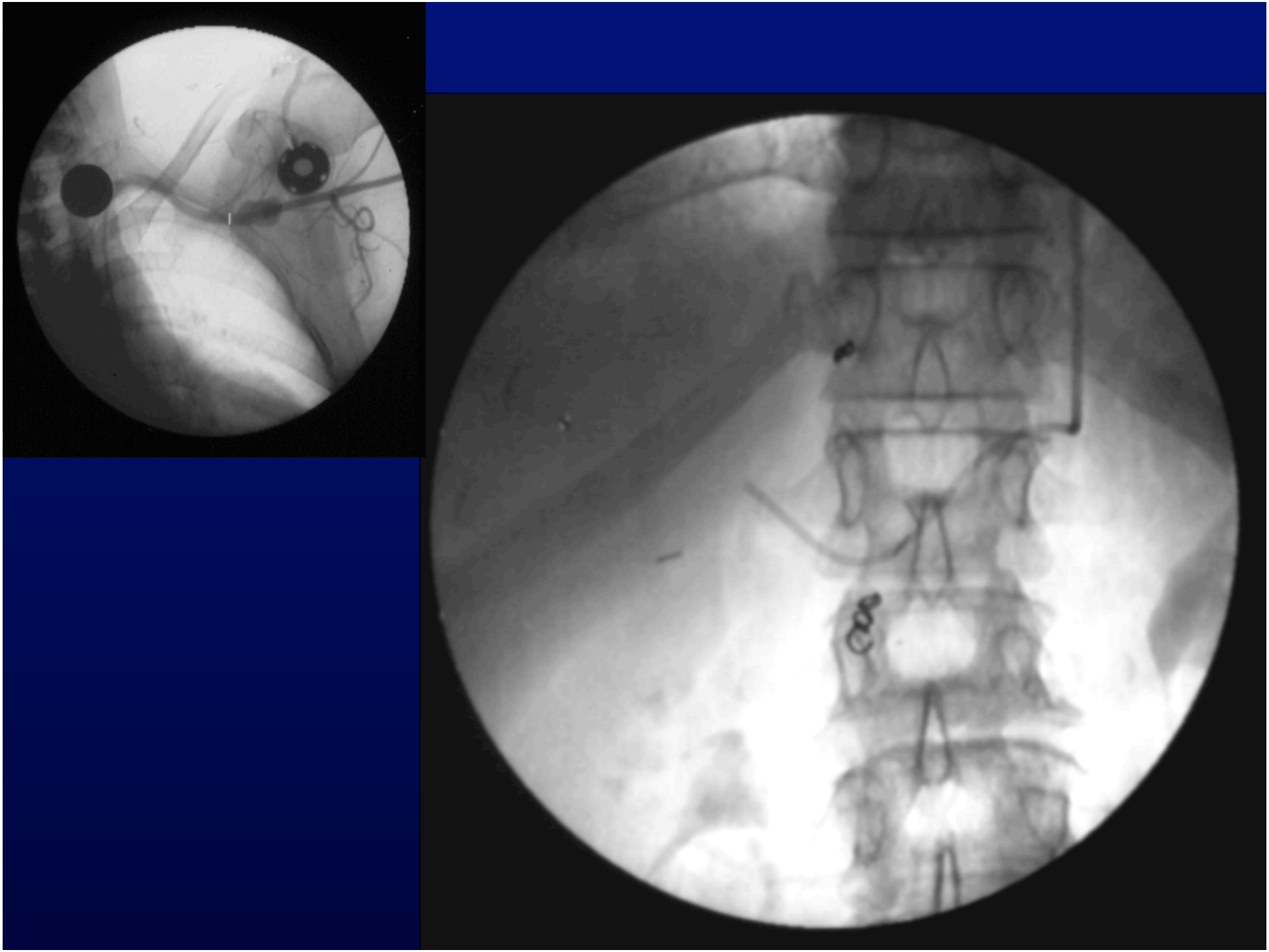
Karatzas A, Katsanos K, Maroulis I, Kalogeropoulou C, Tzorakoleftherakis E, Karnabatidis D.

### Abstract

ABSTRACT:

**INTRODUCTION:** Liver metastases are rare in salivary gland tumors and have been reported only once to be the first manifestation of the disease. They are usually treated with surgical resection of the primary tumor and systemic chemotherapy. Drug-eluting bead chemoembolization has an evolving role in the treatment of hepatocellular carcinoma, as well as in the treatment of metastatic disease of the liver. Nevertheless, it has never been used in a patient with salivary gland liver metastases.

- ✓ ***PORT A CATH*** mts metacrone
- ✓ ***CHEMIOINFUSIONE*** fotemustina ***(PERFUSIONE ISOLATA DEL FEGATO)***
- ✓ ***TAE*** NETs
- ✓ ***TACE*** DEBIRI
- ✓ ***TARE*** 90Y
- ✓ ***EMBOLIZZAZIONE PORTALE***



J Chemother. 2011 Oct;23(5):300-5.

# Liver metastases from melanoma: hepatic intra-arterial chemotherapy. A retrospective study.

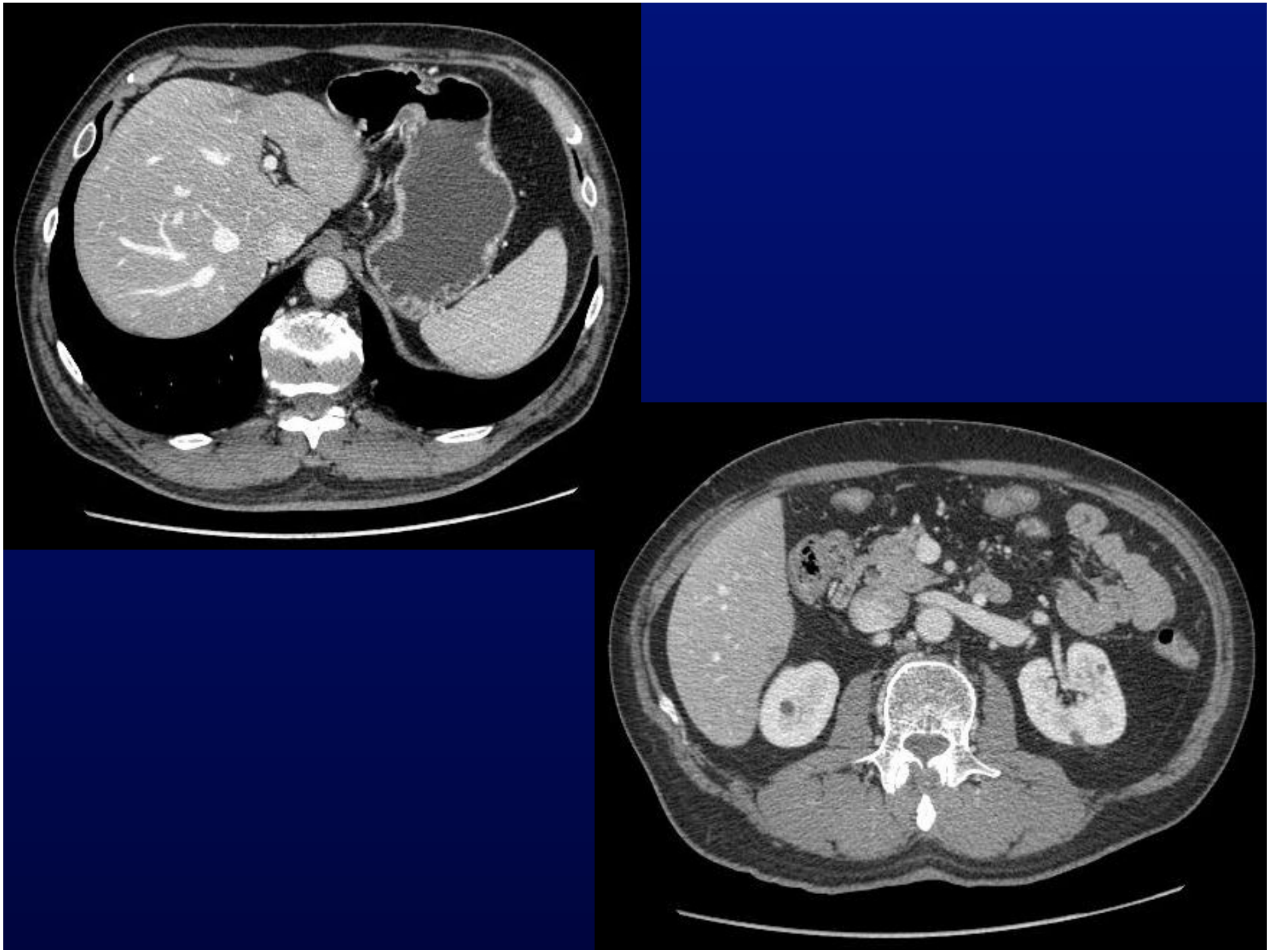
**Farolfi** A, Ridolfi L, Guidoboni M, Milandri C, Calzolari F, Scarpi E, Amadori D, Ridolfi R.

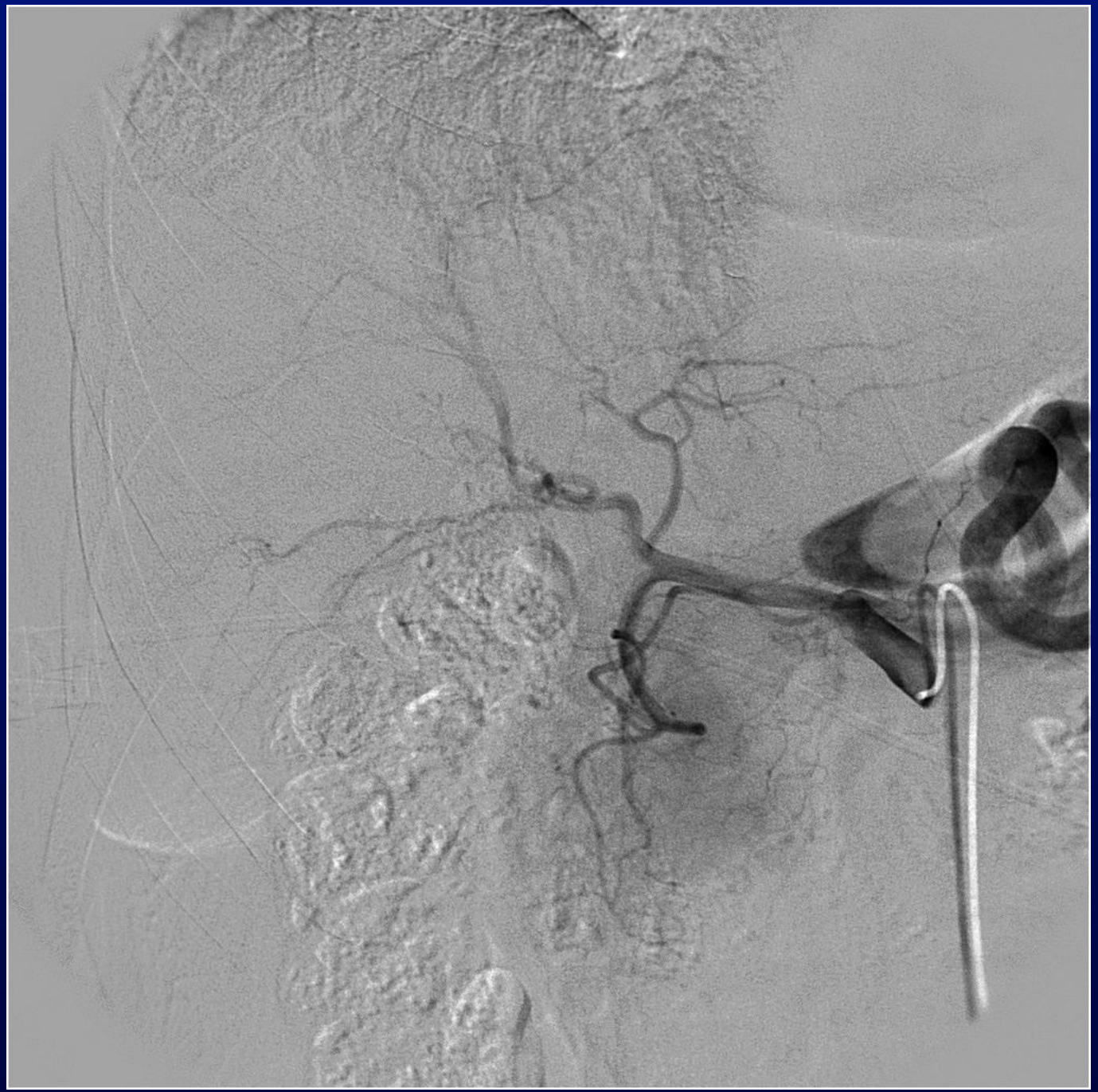
Department of Oncology, Instituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Meldola, Italy.

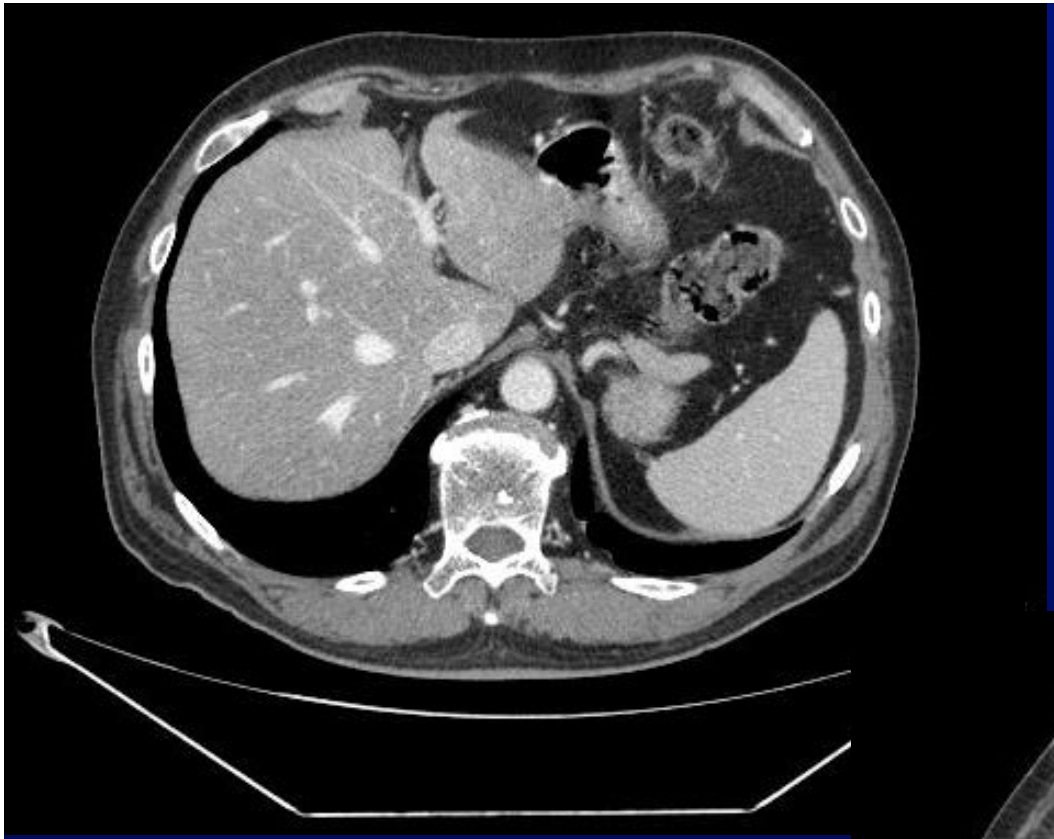
## Abstract

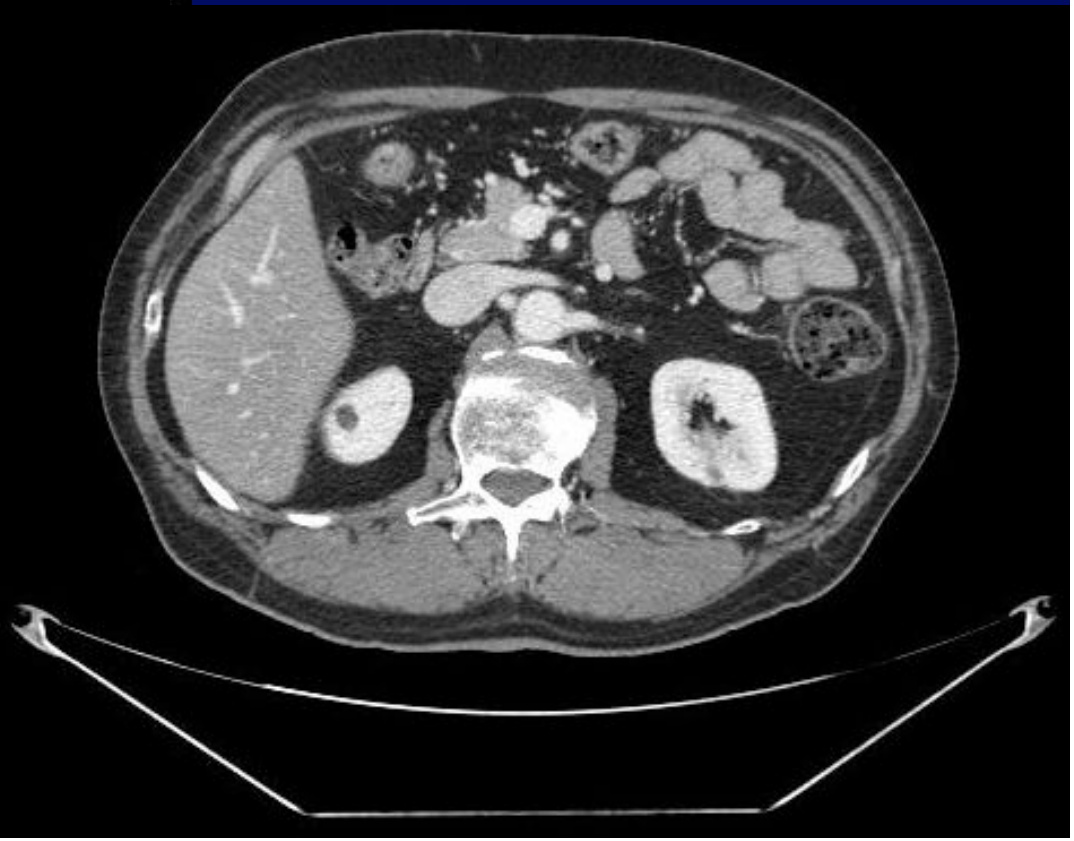
The **liver** is the primary site of **metastases** in most uveal **melanoma** patients. We retrospectively investigated intraarterial chemotherapy (IAC) as treatment for patients with hepatic **melanoma metastases**.Twenty-three patients (18 with uveal **melanoma**) received fotemustine (14 patients, 61.9%) or carboplatin (9 patients, 31.1%) via hepatic IAC delivery. The catheter was introduced through percutaneous access to the femoral artery with drugs delivered directly to the hepatic artery, and was removed at the end of each treatment cycle. A total of 3 cycles was planned, repeated every 21 days. However, patients with a clinical response could receive more than 3 cycles, provided that the toxic effects were acceptable.IAC was well tolerated and no catheter-related complications or grade 4 toxicities were reported. Considering only uveal **melanoma** patients, the overall response rate and disease control rate was 16.7% and 38.9%, respectively. Median time to progression was 6.2 months (95% CI 3.7-10.5) and median overall survival was 21 months (95% CI 8-39).IAC is well tolerated and is a valid choice for patients with a poor prognosis since median survival rates are among the longest reported.

PMID: 22005064 [PubMed - indexed for MEDLINE]









Int J Clin Oncol. 2012 Aug;17(4):306-15. doi: 10.1007/s10147-012-0445-1. Epub 2012 Jul 18.

# Current status of embolic agents for liver tumor embolization.

Osuga K, Maeda N, Higashihara H, Hori S, Nakazawa T, Tanaka K, Nakamura M, Kishimoto K, Ono Y, Tomiyama N.

Department of Diagnostic and Interventional Radiology, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita, Osaka, 565-0871, Japan. osuga@radiol.med.osaka-u.ac.jp

Particulate embolic agents for interventional oncology

| Category | Devices (company) | Composition |
|---|---|---|
| Conventional particles | Gelpart (Nippon Kayaku) | Porous gelatin particles |
| | PVA (Cook) | Non-spherical PVA |
| Bland microspheres | Embosphere (Merit Medical) | Trisacryl polymer embedded with gelatin |
| | Bead Block (Biocompatibles) | Spherical PVA |
| | Contour SE (Boston Scientific) | Spherical PVA |
| | Embozene (Celonova) | Polyphosphazene-coated PMMA |
| Drug-eluting microspheres | DC Bead/LC Bead (Biocompatibles) | PVA modified by sulfonate sodium salt |
| | HepaSphere/QuadraSphere (Merit Medical) | SAP microsphere |

*PVA* polyvinyl alcohol, *PMMA* polymethylmethacrylate, *SAP* superabsorbent polymer

Radiographics. 2008 Jul-Aug;28(4):1131-45. doi: 10.1148/rg.284075170.

# Neuroendocrine tumors: role of interventional radiology in therapy.

Steward MJ, Warbey VS, Malhotra A, Caplin ME, Buscombe JR, Yu D.

Department of **Radiology**, Royal Free Hospital, Pond Street, London NW3 2QG, England.
MichaelSteward@doctors.net.uk

## Abstract

The management of **neuroendocrine tumors** (NETs) is complex. Although NETs can affect a variety of organ systems, hepatic metastatic disease in particular lends itself to a wide range of **interventional** treatment options. Prior detailed radiologic assessment and careful patient selection are required. Curative surgery should always be considered but is rarely possible. Embolization, radionuclide **therapy**, or ablative techniques may then be undertaken. Transcatheter arterial embolization (TAE) may be used alone or in combination with transcatheter arterial chemoembolization (TACE). NET type and extent of hepatic involvement are factors that can help predict the success of either TAE or TACE. Embolization techniques can also be useful in patients with nonhepatic NETs. Radionuclide **therapy** is emerging as a valuable adjunct and is dependent on positive somatostatin receptor status. Therapeutic radiopeptides may be delivered arterially. Ablative techniques have been shown to play a **role** in the palliation of symptoms and principally involve radiofrequency ablation. Hepatic cryotherapy and percutaneous ethanol injection have also been used. A multidisciplinary approach to treatment and follow-up is important. Imaging should involve dual-phase multidetector computed tomography and contrast material-enhanced magnetic resonance imaging. The **role** of the **interventional** radiologist will continue to expand as imaging techniques become more refined.

PMID: 18635633 [PubMed - indexed for MEDLINE] **Free full text**

# cTACE

**Conventional**
**Transcatheter Arterial**
**Chemo Embolization**

*Somministrazione intra-arteriosa di LIpiodol + chemioterapico ed embolizzazione con particelle riassorbibili.*

# pTACE

**Precision Transcatheter Arterial**
**Chemo Embolization**

*Somministrazione intra-arteriosa di microsfere non riassorbibili a rilascio controllato di chemioterapico.*

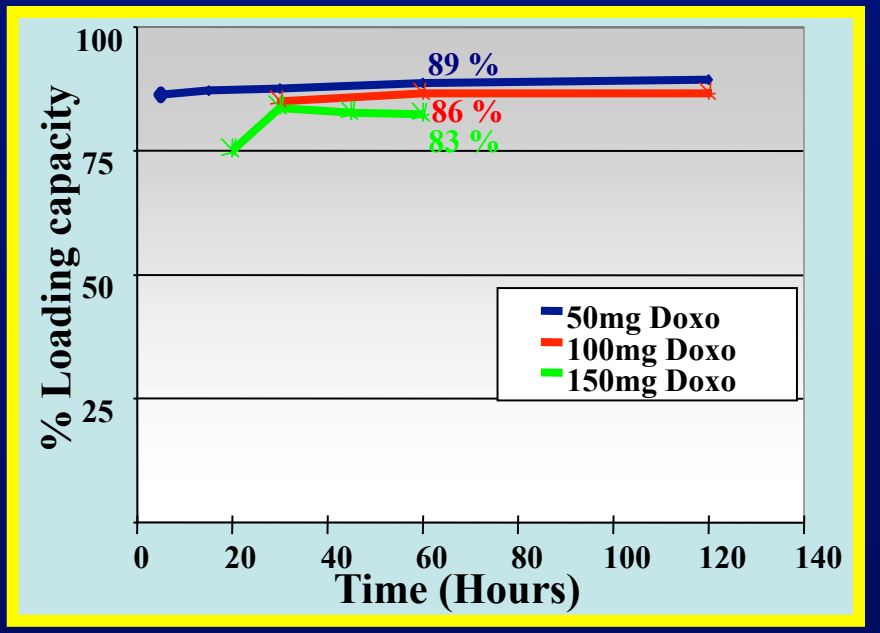
# pTACE: razionale

- Trattamento superselettivo del solo nodulo tumorale mediante l'utilizzo di un nuovo materiale embolizzante **non riassorbibile**, idrofilo, precalibrato e biocompatibile (**Hepasphere, DCBead**).
- Espandibilità delle hepasphere (x4 rispetto al volume a secco).
- Deformabilità (non traumatica) e plasticità nel contesto del lume vasale, dopo l'aumento dimensionale.
- Ottimale assorbimento del chemioterapico (doxorubicina) e rilascio controllato.

## Hepaspheres + Doxorubicina

- Microsfere caricate negativamente (polimero anionico)
- Forti interazioni con chemioterapici caricati positivamente come la Doxorubicina; la tossicità sistemica si riduce.

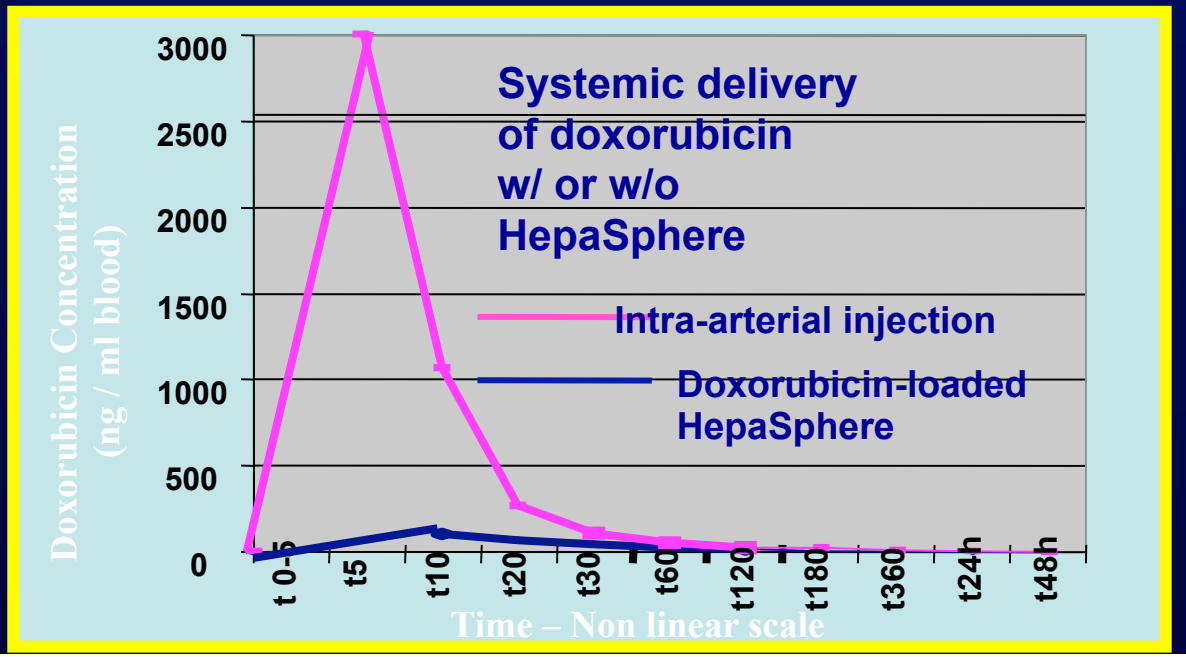
Capacità di assorbimento della Doxorubicina




Valutazione in vivo della concentrazione sistemica di chemioterapico.

- 25mg di HepaSphere possono essere caricati con 125 mg Doxorubicina

- 30 minuti sono sufficienti per caricare il 95%della soluzione di Doxorubicina.

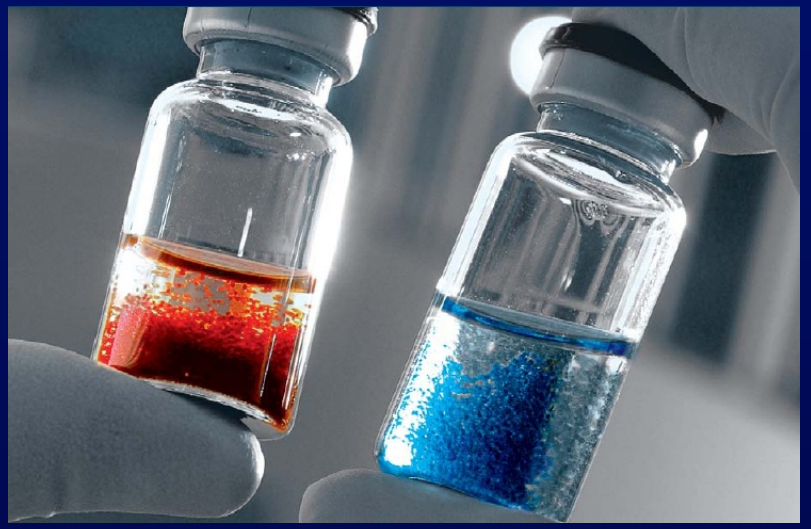


# ...evoluzione della TACE

*Si è sviluppato il concetto del*
**Drug-Eluting Beads**

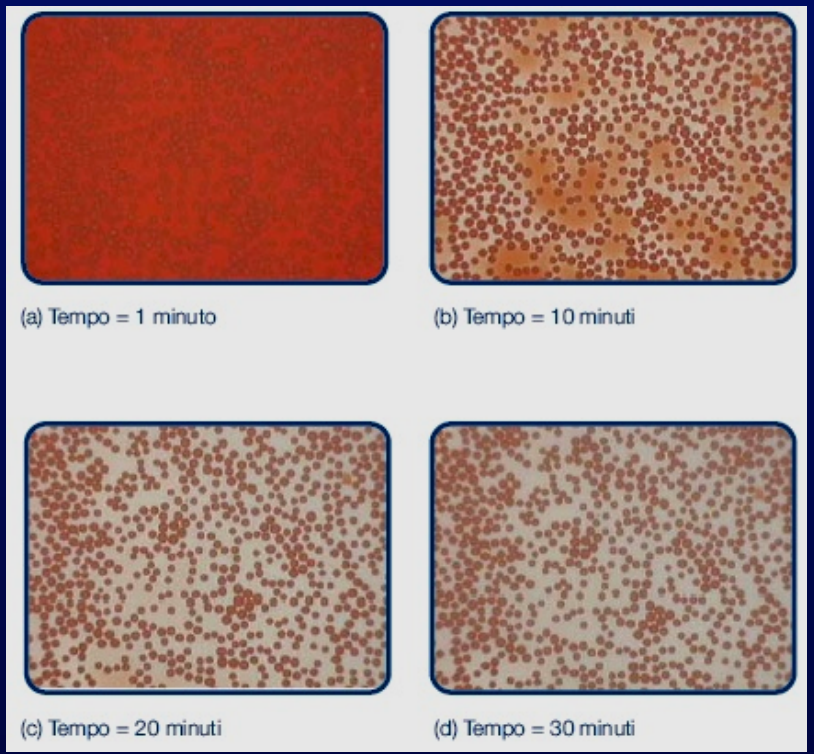
## DC BEAD

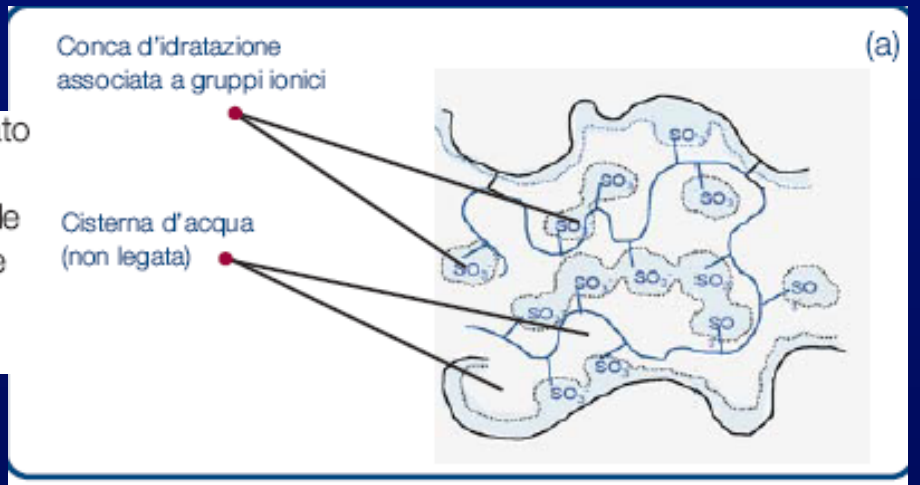
- *Microsfere a rilascio di farmaco,a bassa compressività in grado di essere caricate con chemioterapici a dosi elevate, che rilasciano poi in maniera controllata.*
- *Approvate con il marchio CE*
- *Nuovo polimero idrogel, sulfonato-modificato, con tecnologia N-Fil*
- *Colorate di blue*
- *Disponibili in una gamma di misure:*
  - *100-300µm*
  - *300-500µm*
  - *500-700µm*

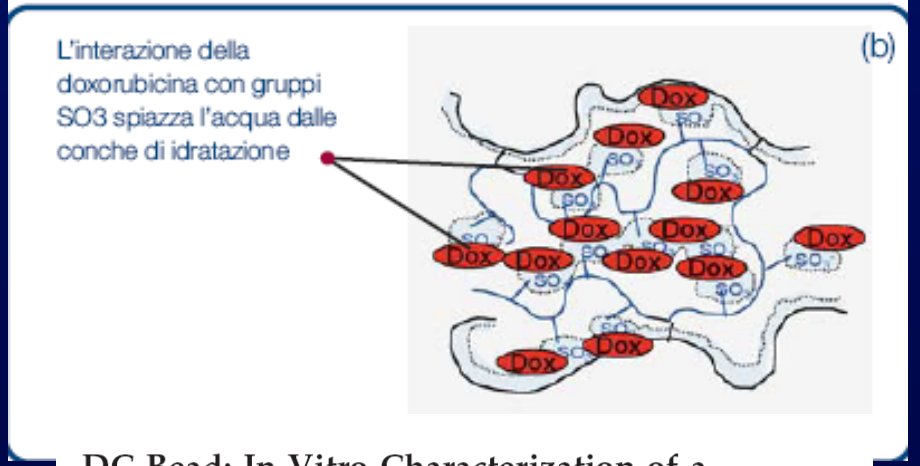


# Drug Eluting Beads

Le microsfere sono composte da un idrogel sulfonato-modificato e sono cariche negativamente, mentre i farmaci, che hanno un'ammina che è protonata quando il farmaco è in forma di sale cloridrato, hanno una carica complessiva positiva. L'interazione elettrostatica tra le specie a carica opposta è il meccanismo di caricamento delle DC Bead.




**DC Bead: In Vitro Characterization of a Drug-delivery Device for Transarterial Chemoembolization**

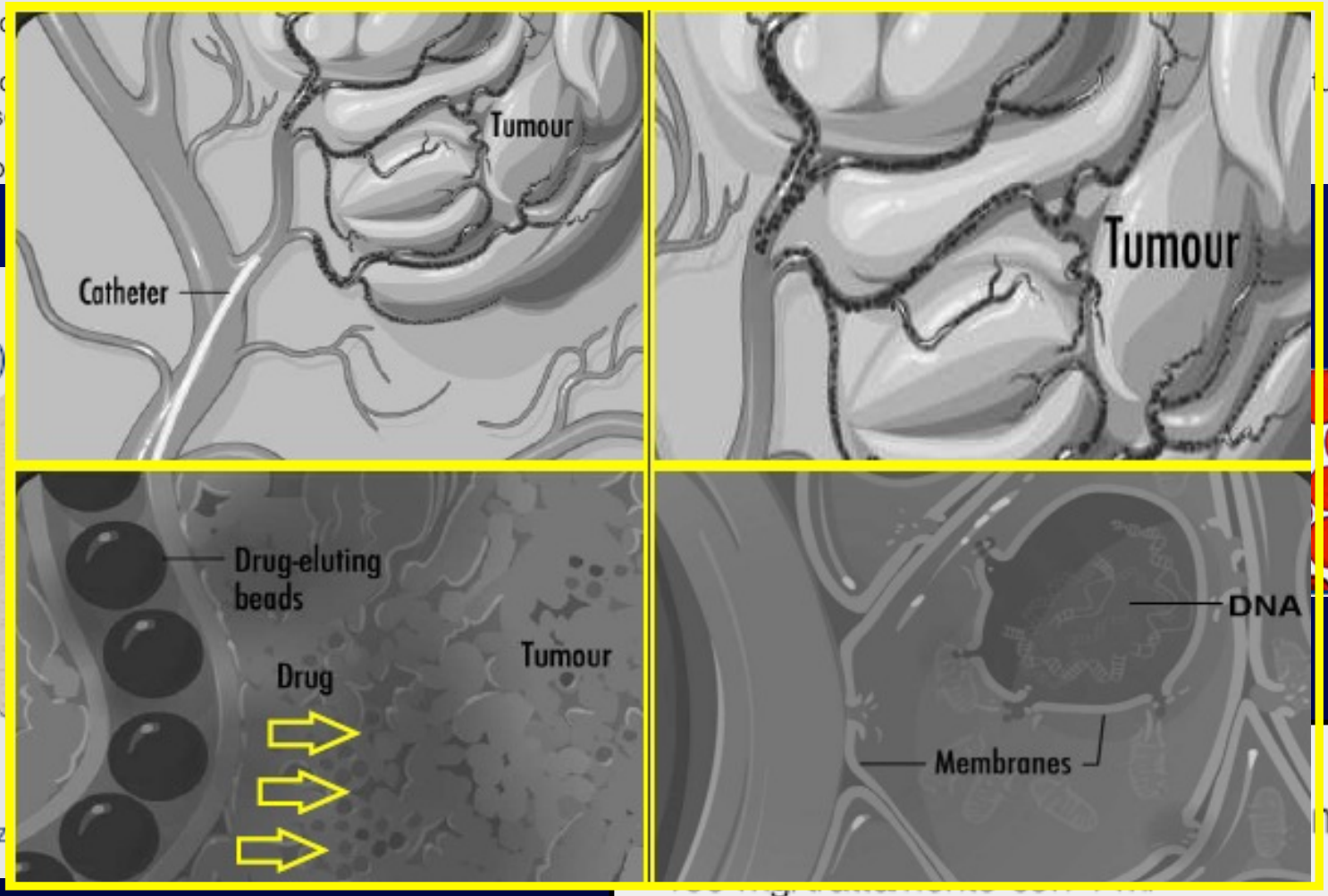
Andrew L. Lewis, PhD, M. Victoria Gonzalez, Andrew W. Lloyd, PhD, Brenda Hall, PhD, Yiqing Tang, PhD, Sean L. Willis, PhD, Simon W. Leppard, DPhil, Laura C. Wolfenden, Rosemary R. Palmer, and Peter W. Stratford, PhD

# Drug Eluting Beads

Concetto delle microsfere a rilascio di farmaco

- Le mic
- Le mic
  divers
- Il vaso

umorali per




(a)

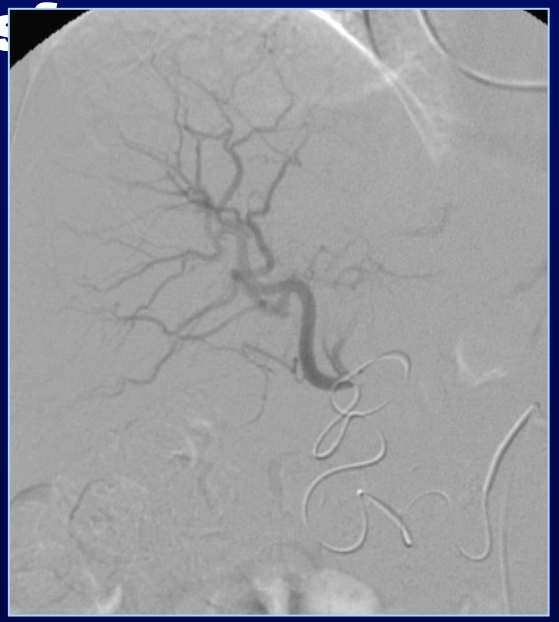

Fig 1. Az

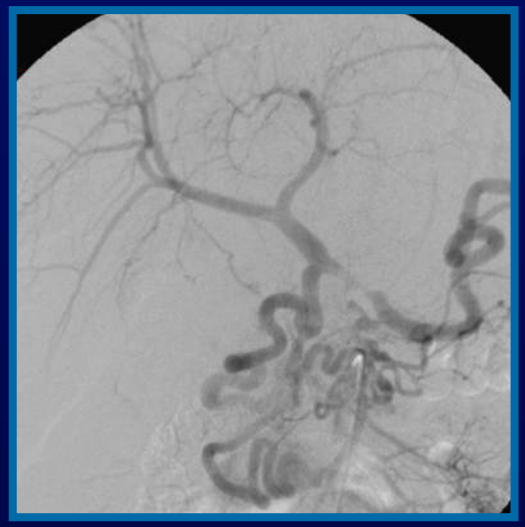
mg/ml e di

# DEBIRI

E’ raccomandabile l’uso di un **microcatetere**:

- Riduce il vasospasmo
- Permette il cateterismo di arterie difficili
- Permette un’ottima distribuzione delle micros





**Infusione molto lenta delle microsfere**

# DEBIRI Colorectal L.M

## *Farmaci Peri-Proceduralì*

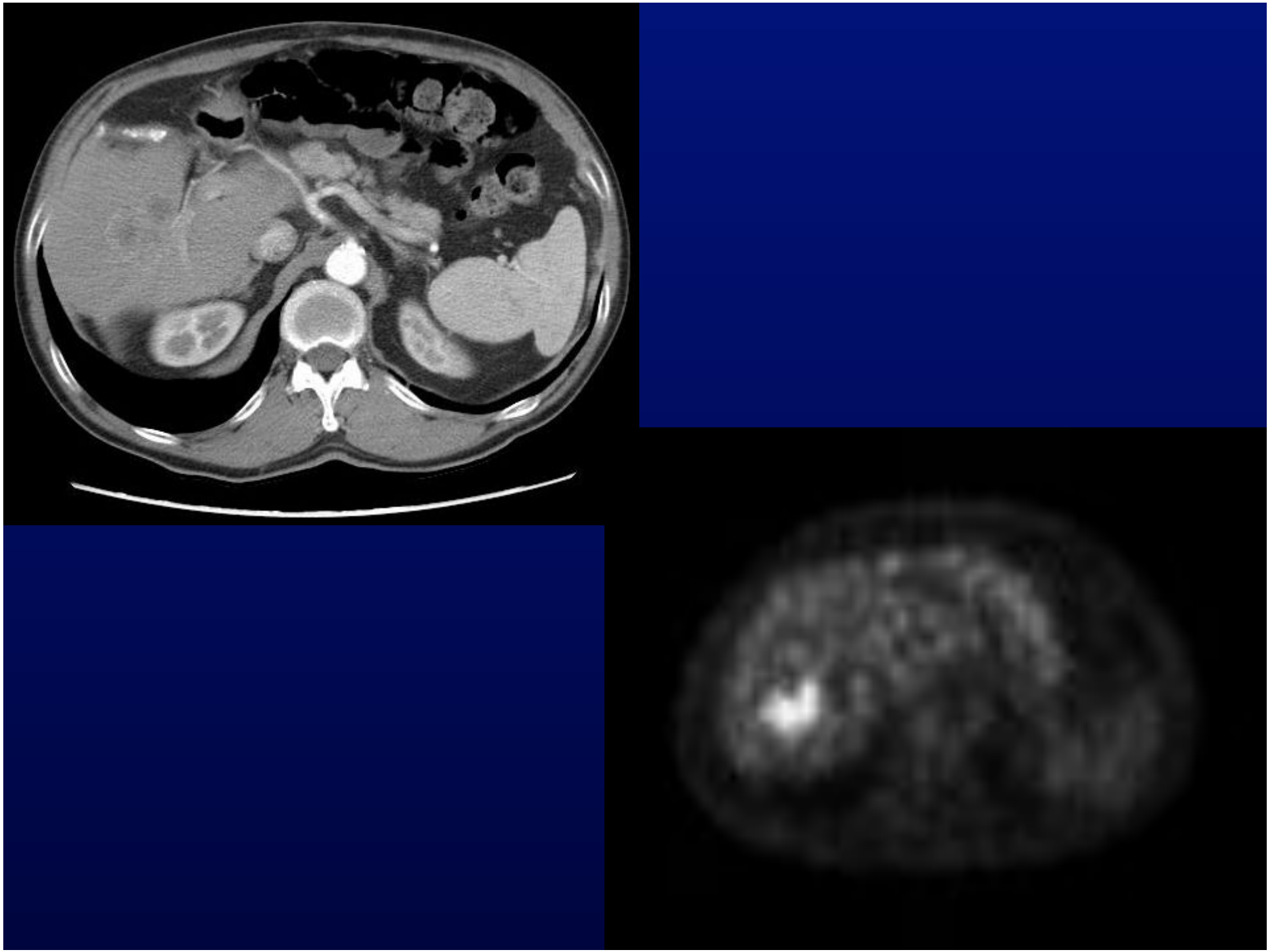
## Farmaci per il dolore:

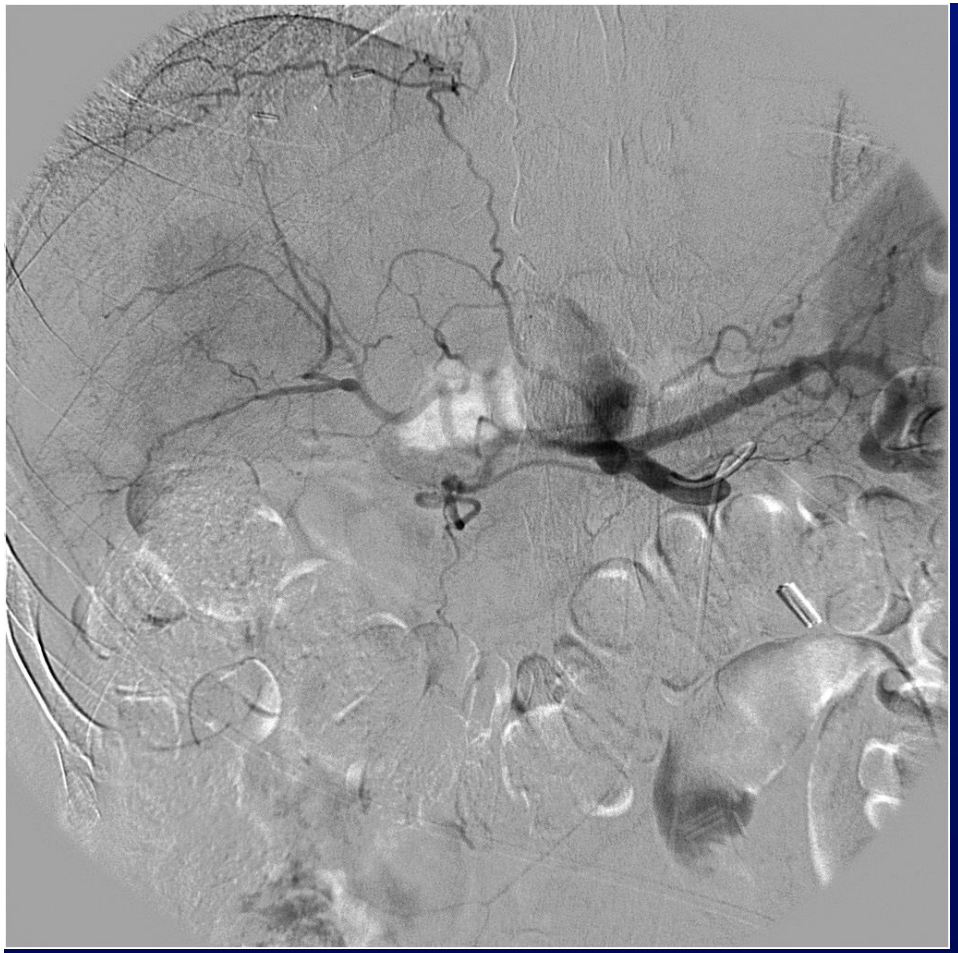
- 1 fiala (10mg) di Morfina/100ml di soluzione fisiologica e.v 30 min. prima della procedura
- 1 fiala di Morfina/100ml di soluzione fisiologica e.v in infusione lenta durante la TACE
- 1 fiala di Morfina/100ml di soluzione fisiologica e.v in infusione molto lenta dopo la procedura

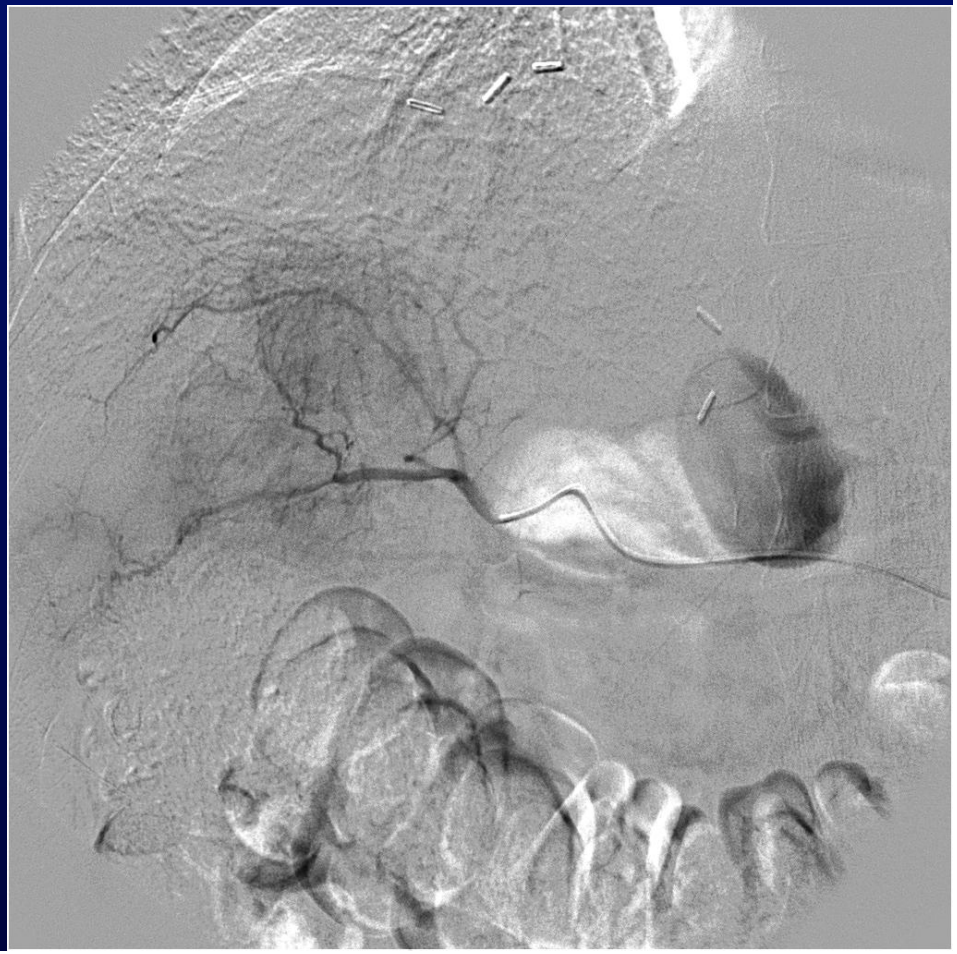
## Trattamento profilattico per la nausea:

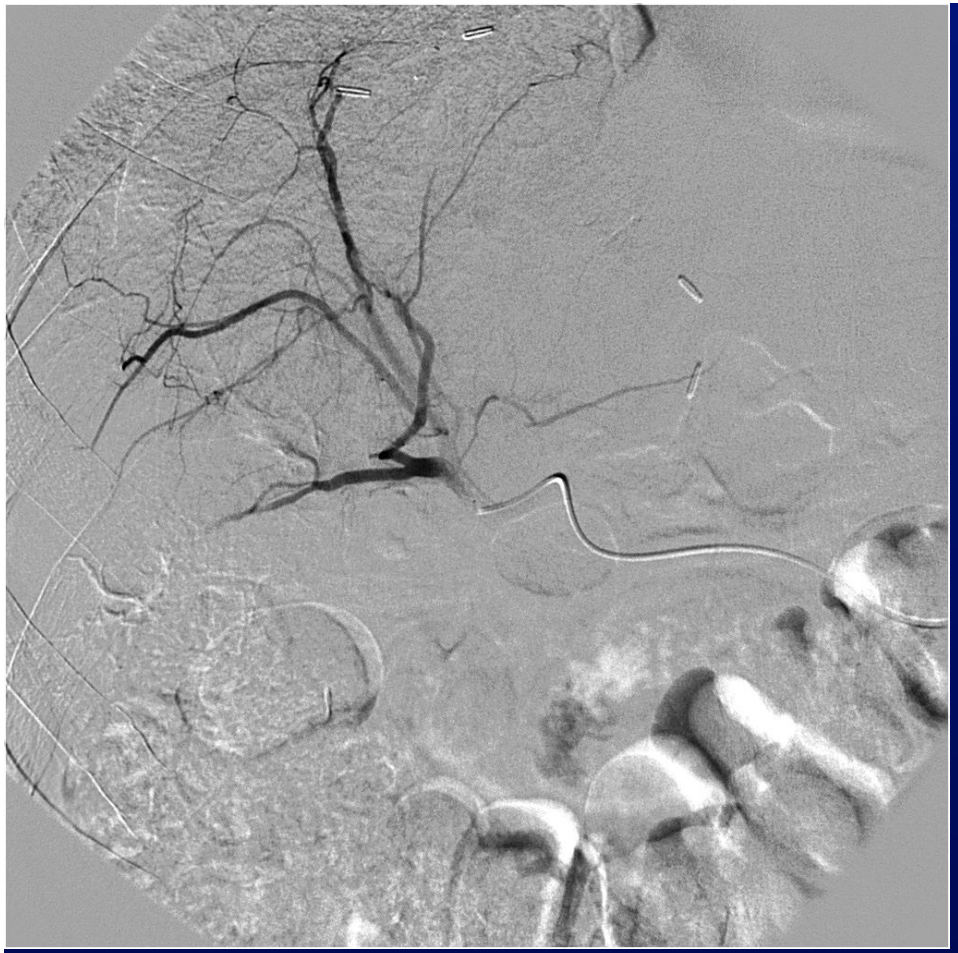
- 1 fiala (5mg) di Tropisetron/100ml di soluzione fisiologica e.v. prima della TACE e a 6 ore

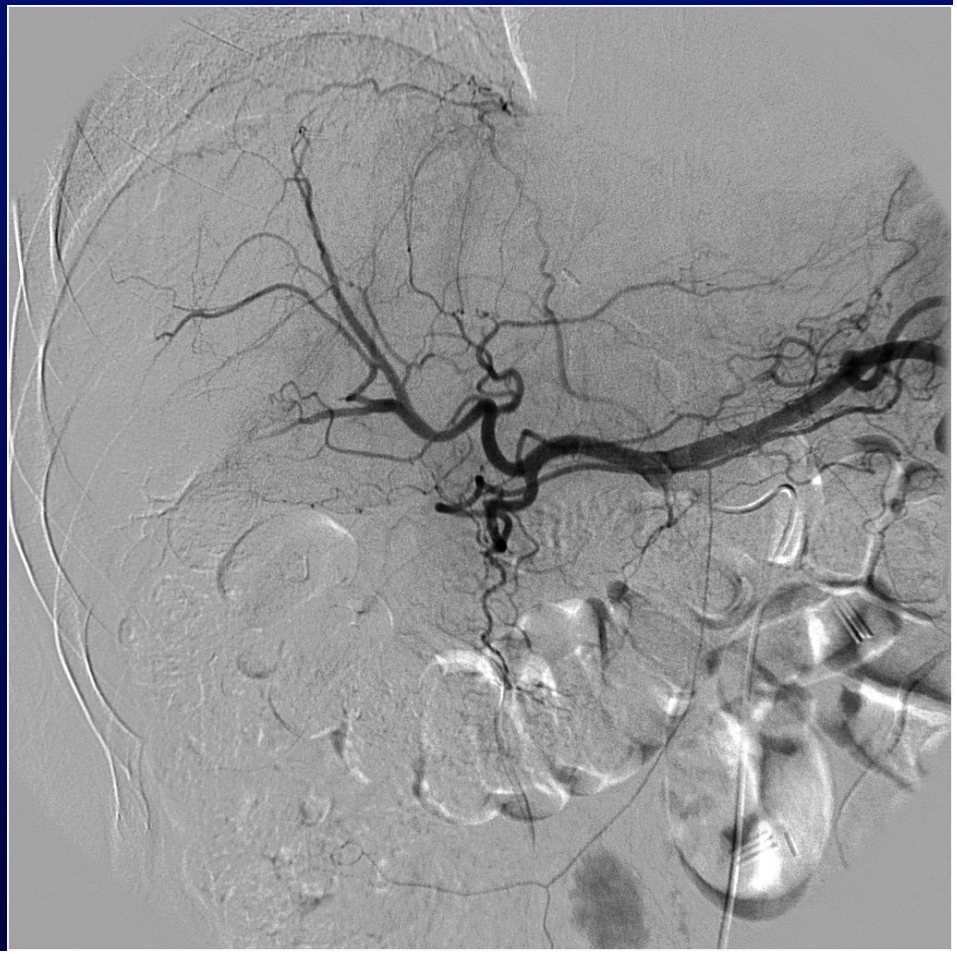
***La profilassi antibiotica e la protezione gastrica devono essere somministrate dal giorno 0 al giorno 5.***

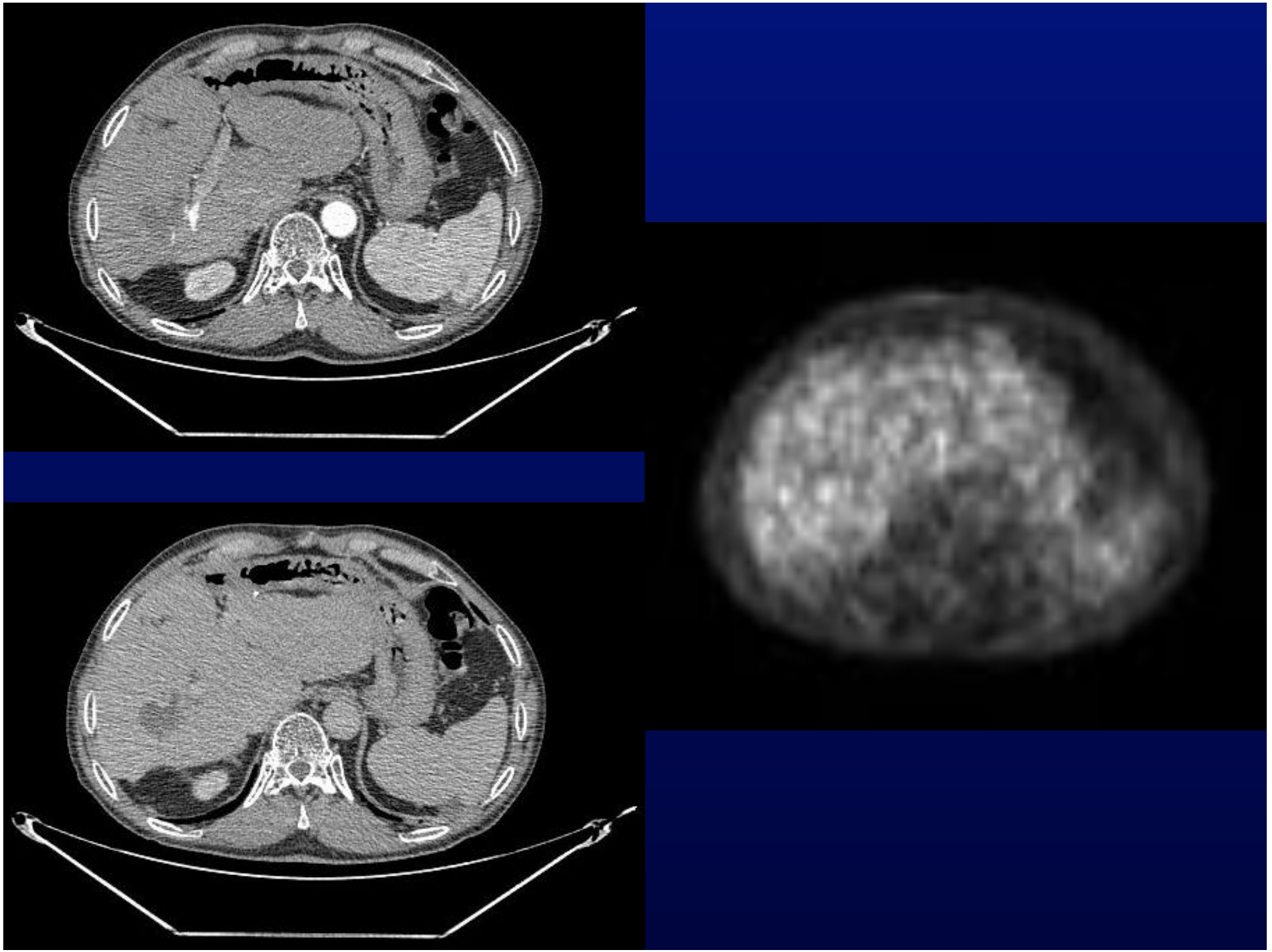






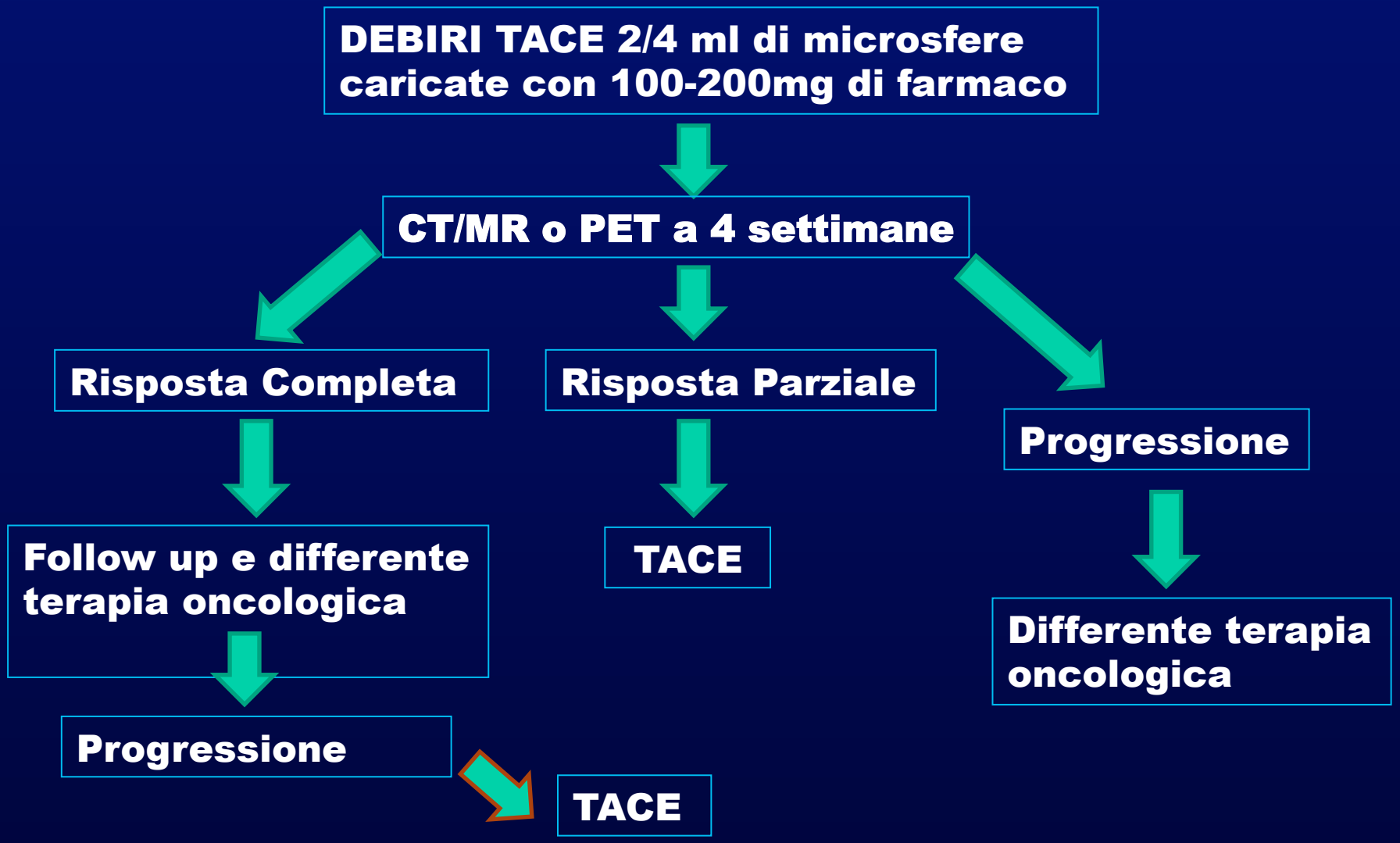






# DEBIRI Colorectal L.M

## DEBIRI algoritmo di trattamento delle metastasi epatiche da colon-retto



Anticancer Res. 2012 Apr;32(4):1387-95.

# Intra-arterial infusion of irinotecan-loaded drug-eluting beads (DEBIRI) versus intravenous therapy (FOLFIRI) for hepatic metastases from colorectal cancer: final results of a phase III study.

Fiorentini G, **Aliberti C**, Tilli M, Mulazzani L, Graziano F, Giordani P, Mambrini A, Montagnani F, Alessandroni P, Catalano V, Coschiera P.

Department of Oncology-Hematology, Azienda Ospedaliera Ospedali Riuniti Marche Nord, Pesaro, Italy. g.fiorentini@alice.it

## Abstract

**BACKGROUND:** Metastases to the liver receive most of their blood supply from the arterial route, therefore for patients with hepatic metastases from large bowel cancer, hepatic arterial infusion adopting drug-eluting beads preloaded with irinotecan (DEBIRI) may offer a chance of cure.

**PATIENTS AND METHODS:** In a multi-institutional study, 74 patients were randomly assigned to receive DEBIRI (36) versus systemic irinotecan, fluorouracil and leucovorin (FOLFIRI, 38). The primary end-point was survival; secondary end points were response, recurrence, toxicity, quality of life, cost and influence of molecular markers.

**RESULTS:** At 50 months, overall survival was significantly longer for patients treated with DEBIRI than for those treated with FOLFIRI (p=0.031, log-rank). Median survival was 22 (95% Confidence Interval CI=21-23) months, for DEBIRI and 15 (95% CI=12-18) months for FOLFIRI. Progression-free survival was 7 (95% CI=3-11) months in the DEBIRI group compared to 4 (95% CI=3-5) months in the FOLFIRI group and the difference between groups was statistically significant (p=0.006, log-rank). Extrahepatic progression had occurred in all patients by the end of the study, at a median time of 13 (95% CI=10-16) months in the DEBIRI group compared to 9 (95% CI 5-13) months in the FOLFIRI group. A statistically significant difference between groups was not observed (p=0.064, log-rank).The median time for duration of improvement to quality of life was 8 (95% CI=3-13) months in the DEBIRI group and 3 (95% CI=2-4) months in the FOLFIRI group. The difference in duration of improvement was statistically significant (p=0.00002, log-rank).

**CONCLUSION:** This study showed a statistically significant difference between DEBIRI and FOLFIRI for overall survival (7 months), progression-free survival (3 months) and quality of life (5 months). In addition, a clinically significant improvement in time to extrahepatic progression (4 months) was observed for DEBIRI, a reversal of the expectation for a regional treatment. This suggests a benefit of DEBIRI treatment over standard chemotherapy and serves to establish the expected difference between these two treatment options for planning future large randomized studies.

PMID: 22493375 [PubMed - indexed for MEDLINE]

| Response | DEBIRI (n=35) | FOLFIRI (n=35) |
|---|---|---|
| Complete + partial | 24 (68.6%) | 7 (20%) |
| Stable disease | 4 (11.4%) | 12 ( 34.3%) |
| Progression | 7 (20%) | 16 (45.7%) |

| Toxicity (Grade 2 and 3) | DEBIRI (% out of 70 cycles delivered) | FOLFIRI (% out of 277 cycles delivered) |
|---|---|---|
| Pain | 30% | 0% |
| Vomiting | 25% | 25% |
| Diarrhea | 2% | 35% |
| Asthenia | 20% | 50% |
| Leukopenia | 5% | 35% |
| Anaemia | 5% | 35% |
| Fever | 15% | 3% |
| Alopecia | 5% | 35% |

# **Y90** Radioembolizzazione

- Le microsfere di Y90 sono particelle di 20-40 μm che emettono **radiazioni β**, distribuite mediante l'arteria epatica
- L'algoritmo di trattamento è analogo a quello seguito per la TACE

- **TACE convenzionale → 300-700 µm**


- **DEB-TACE → 100-700 µm**

- **Microsfere radioattive → 20-40µm**

# **SIRT** (Selective internal radiation therapy): **Razionale**

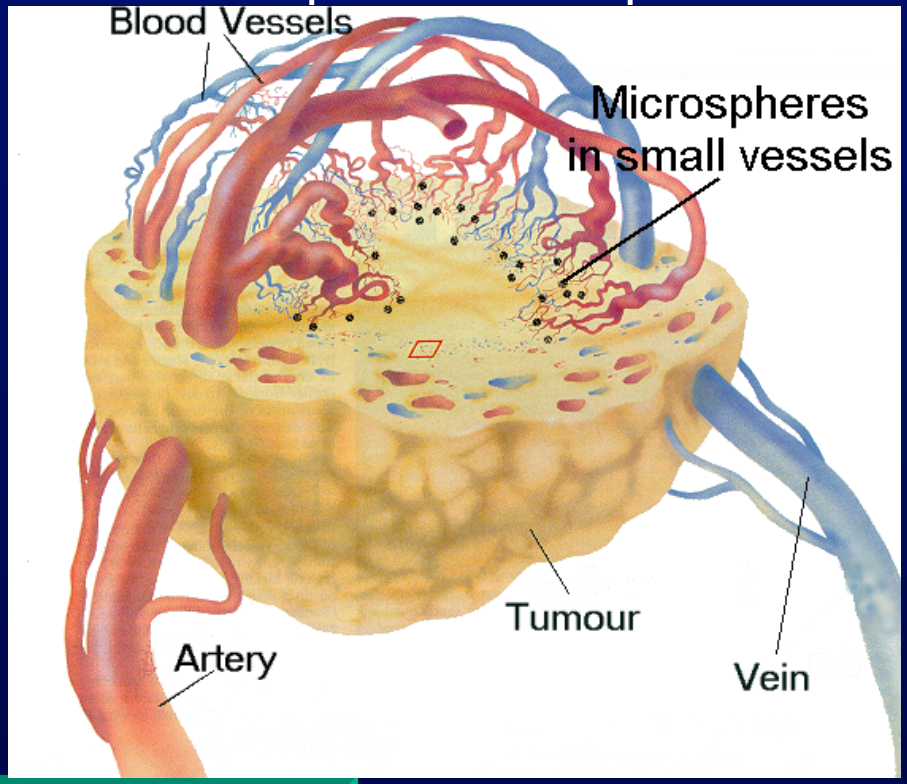
- Somministrazione locale intra-arteriosa di microsfere caricate con Ittrio 90.
- Isotopo che emette raggi beta puri di alta energia senza emissioni di raggi gamma primari.
- Energia media è di 0.9367 MeV.
- Il percorso di questi raggi nei tessuti è mediamente di 2,5 mm (massimo 11 mm).
- **Massima azione a livello della massa tumorale, bassa esposizione dei tessuti vicini.**

Maggiore concentrazione delle microsfere radioisotopiche nelle sedi coinvolte da malattia.

# Razionale Radioembolizzazione

veicoli adatti alla distribuzione selettiva di dosi molto elevate di radiazioni al tumore, mentre l'esposizione alle radiazioni del parenchima epatico normale rimane entro limiti tollerabili

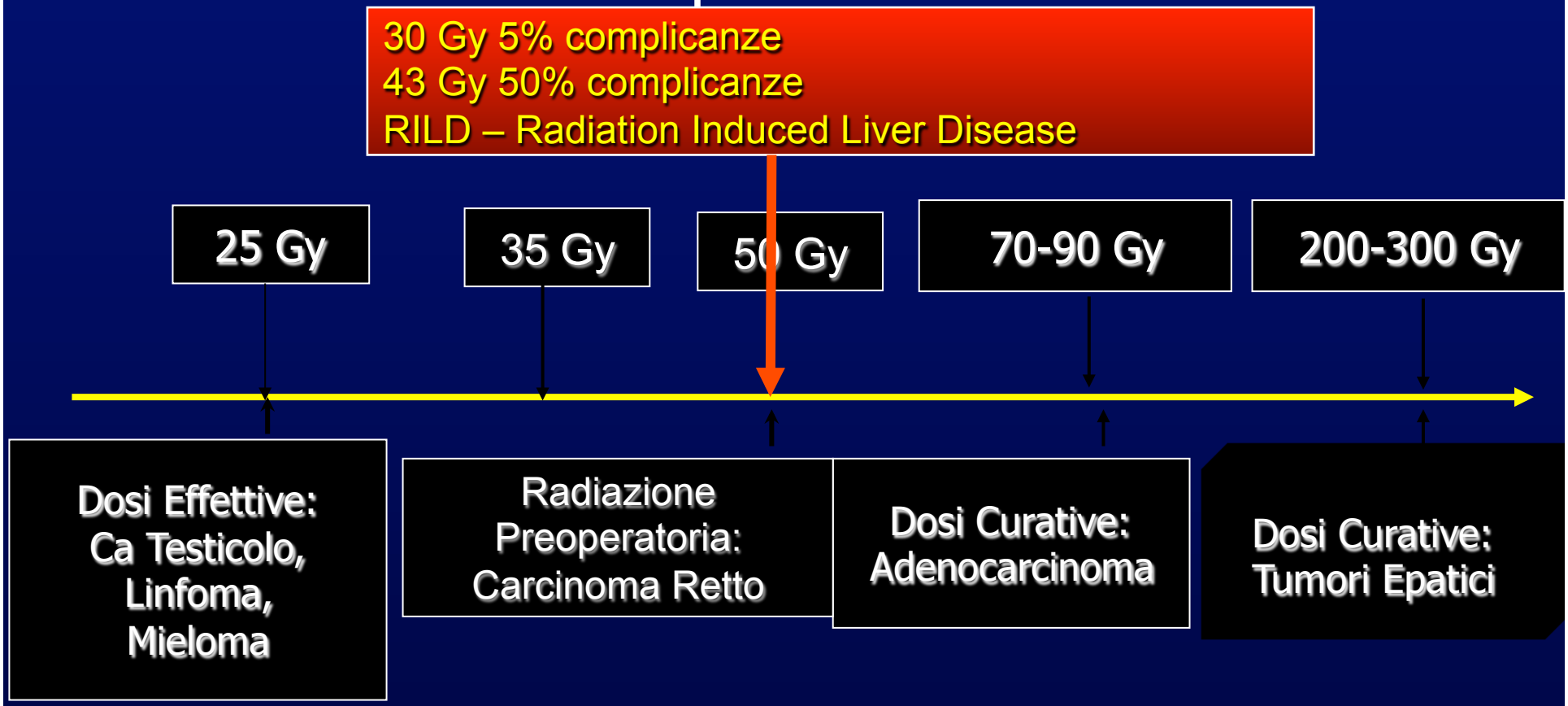
**Microsfere: 20-40 µm**




- Diametro dei vasi tumorali di 25 µm-75 µm
- Diametro delle arteriole terminali di 8-20 µm

# Razionale Radioembolizzazione

## Tolleranza Epatica alla Radiazione

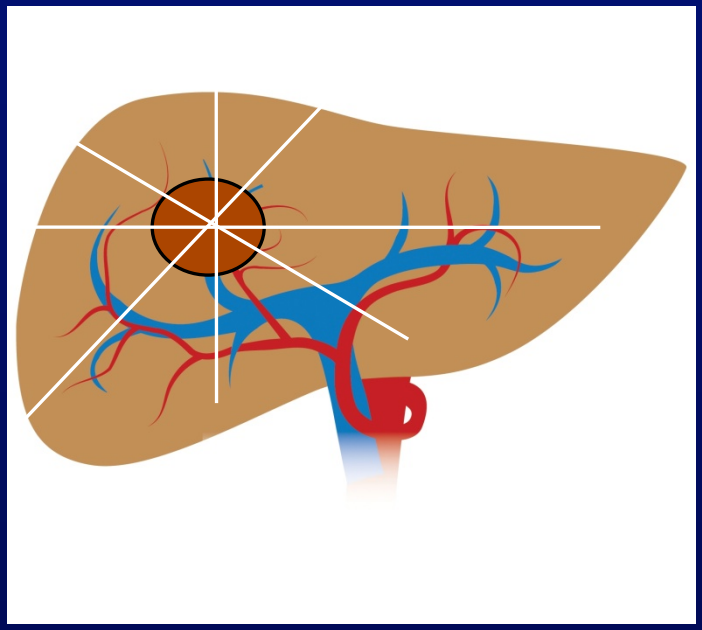


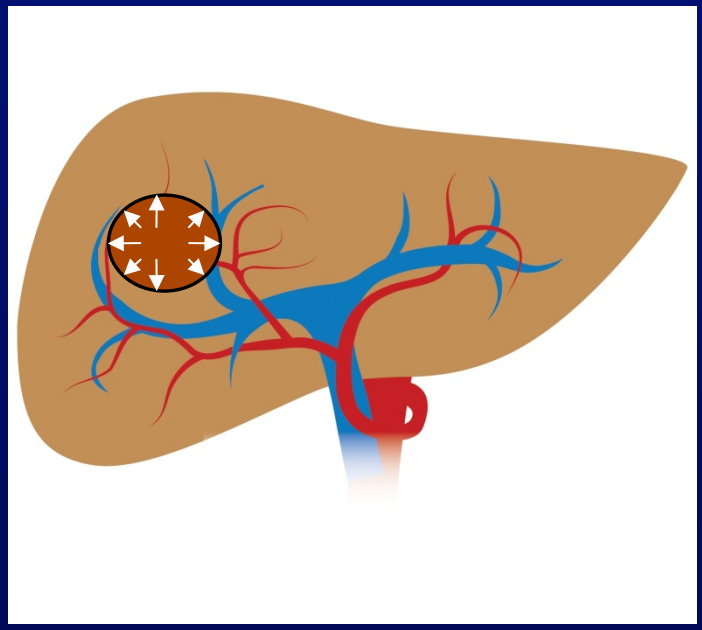

*Dawson LA et al: Analysis of radiation-induced liver disease using the Lyman NTCP model. Int J Radiat Oncol Biol Phys 2002,53:810-21*

*Ingold JA et al: Radiation hepatitis. AM J Roentgenol Radium Ther Nucl Med 03: 200-208,1965*

*Lawrence TS et al. Hepatic toxicity resulting from cancer treatment. Int J Radiat Oncol Biol Phys. 31:1237-48, 1995*

# Radiazione Interna: *Radiation from the "Inside-Out"*





Le microsfere di Y90, a differenza delle sorgenti di radiazioni a fascio esterno, sono fonti di radiazioni che si localizzano preferenzialmente nel sistema vascolare peri- ed intra-tumorale:

- **Alta dose al tessuto bersaglio**
- **Minima irradiazione non-target**
- **Bassa esposizione agli organi e alle strutture adiacenti**

Campbell AM et al. Analysis of the distribution of intra-arterial microspheres in human liver following hepatic yttrium-90 microsphere therapy. Phys Med Biol 2000;45:1023–1033.

# The Role of Tumor Vascularity in Predicting Survival after Yttrium-90 Radioembolization for Liver Metastases

J Vasc Interv Radiol 2009; 20:1564–1569

Kent T. Sato, MD, Reed A. Omary, MD, Christopher Takehana, MD, Saad Ibrahim, MD, Robert J. Lewandowski, MD, Robert K. Ryu, MD, and Riad Salem, MD, MBA

- Retrospective study: 137 patients with metastatic liver disease (108 hypervascular and 29 hypovascular tumors). Therasphere.
- Median survival times for these subgroups were 306 days and 284 days (*P* .67).
- Radiographic vascular appearance of liver tumors does not affect survival after radioembolization.
- Therefore, ***hypovascular tumors*** should not be considered contraindicated for radioembolization.

# **SIRT** (Selective internal radiation therapy): **Indicazioni**

- Attualmente sono disponibili due tipologie di microsfere:
- **TheraSphere® (Nordion)**, microsfere di vetro; nelle linee guida della FDA indicate nelle **neoplasie primitive epatiche non resecabili**.
- **SIR-Spheres® (Sirtex)**, microsfere di resina; nelle linee guida della FDA indicate nelle **metastasi (da tumori del colon, neuroendocrini, della mammella)**.
- In Europa notevole sovrapposizione nelle applicazioni.

| Characteristic | Glass Microsphere Device | Resin Microsphere Device |
|---|---|---|
| Number of spheres per dose | | |
| Range | $3–8 \times 10^6$ | $30–60 \times 10^6$ |
| Mean | $4 \times 10^6$ | $50 \times 10^6$ |
| Specific gravity | High | Low |
| Specific activity (Bq per sphere) | 2500 | 50 |
| Institutional review board oversight | Required | Not required |
| FDA approval category | Humanitarian device exemption | Premarket approval |
| Dose variation with tumor volume | No | Yes |
| Hepatopulmonary shunt upper limit (%) | 10 | 20 |
| Solution used for suspension of spheres | Normal saline | Sterile water |
| Adjuvant chemotherapy | No | Yes |

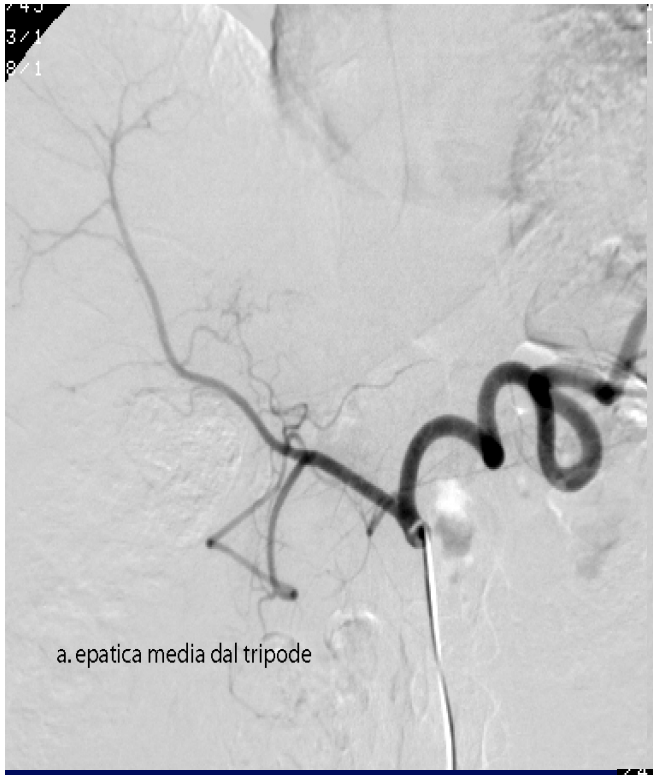
# **SIRT** (Selective internal radiation therapy): **Controindicazioni**

- **Controindicazioni assolute**:
- Elevato shunting epato-polmonare
- Reflussi patologici scintigrafici nel territorio gastro-intestinale

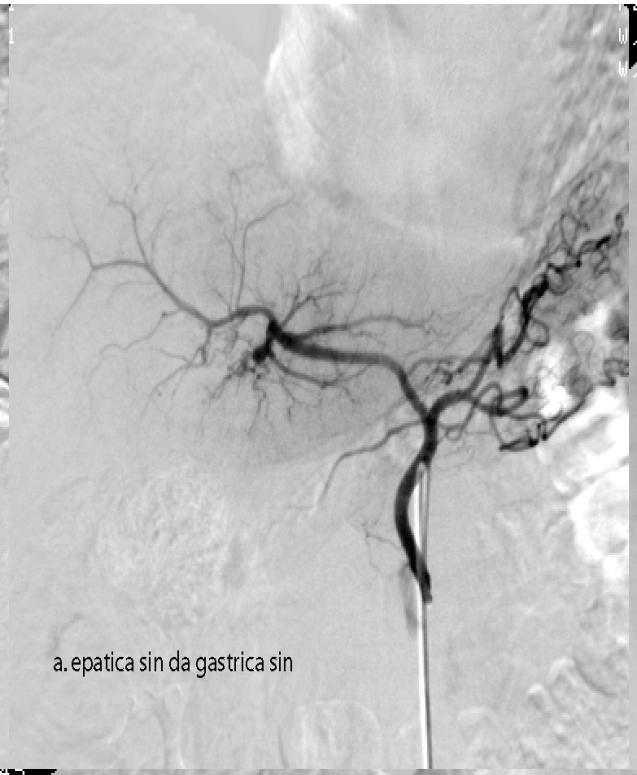
- **Controindicazioni relative**:
- Precedente radioterapia tradizionale stereotassica
- Ascite, elevata bilirubinemia (riserva epatica ridotta)

- La trombosi della vena porta è una controindicazione all'applicazione delle **SIR-Spheres®**, ma non nel caso delle **TheraSphere®.**

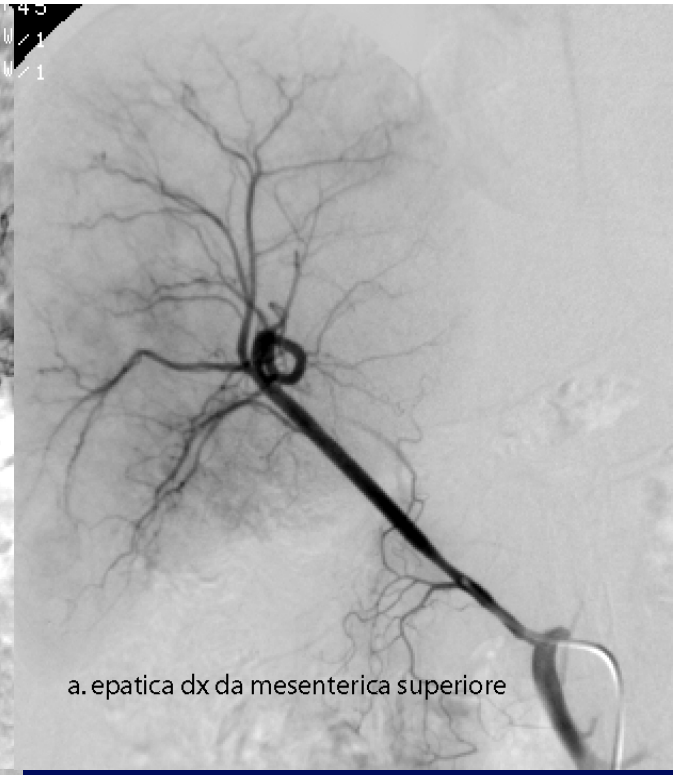

- Salem R, Lewandowski R, Roberts C, et al. Use of yttrium-90 glass microspheres (TheraSphere) for the treatment of unresectable hepatocellular carcinoma in patients with portal vein thrombosis. J Vasc Interv Radiol 2004;15:335–345.



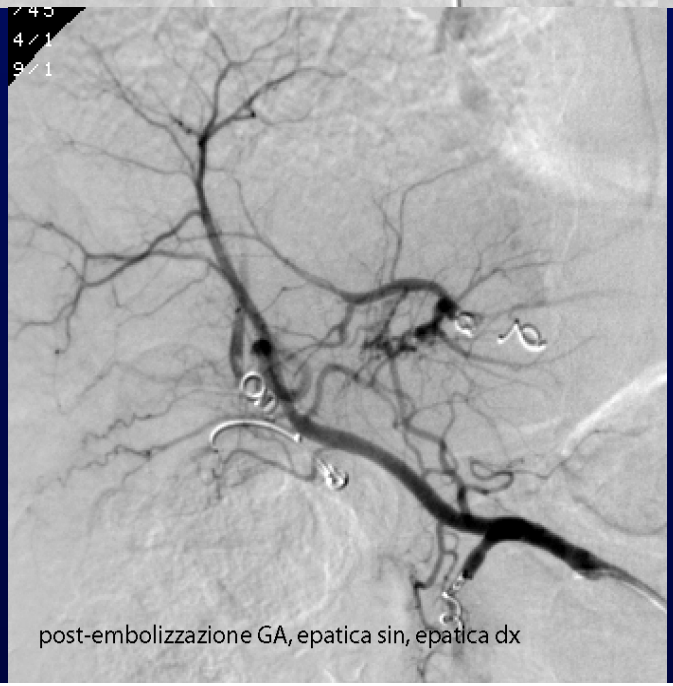
a. epatica media dal tripode



a. epatica sin da gastrica sin

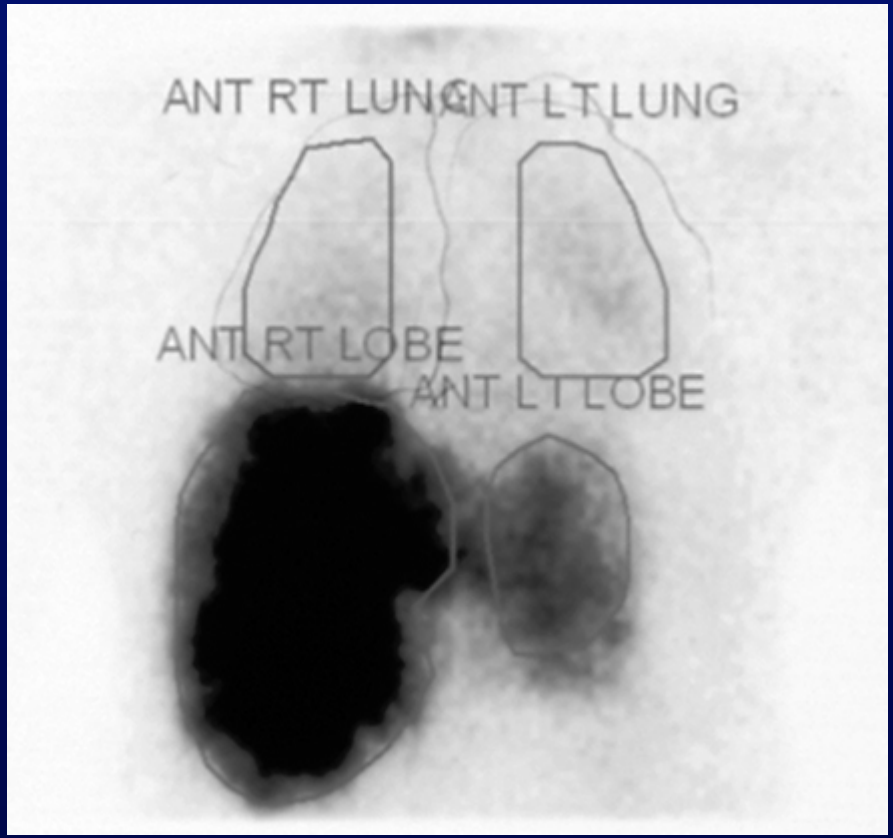


a. epatica dx da mesenterica superiore



post-embolizzazione GA, epatica sin, epatica dx

# **SIRT** (Selective internal radiation therapy): **Tecnica**




Lo shunting epato-polmonare deve essere valutato nel preoperatorio mediante una scintigrafia dopo l'inoculazione di 5–6 mCi (185–222 MBq) di $^{99m}$Tc-MAA (macroaggregati di albumina).

| **A: Calculation of Dose** | |
|---|---|
| Liver Involvement by Tumor (%) | Recommended Dose (GBq) |
| <25 | 2.0 |
| 25–50 | 2.5 |
| >50 | 3.0 |
| **B: Calculation of Dose Reduction** | |
| Hepatopulmonary Shunting (%) | Recommended Dose Reduction (%) |
| <10 | 0 |
| 10–15 | 20 |
| 15–20 | 40 |
| >20 | 100 |

# Flow-chart

**Azienda Ospedaliero-Universitaria di Bologna Policlinico S. Orsola - Malpighi**

**SELEZIONE CANDIDATI**
**(working team)**

**FASE 1:**
**PREPARAZIONE**

TC spirale per volumetria epatica e % fegato coinvolto vs. fegato sano + **TC-PET**

- 1° angiografia : valutazione varianti anatomiche ed eventuale loro embolizzazione (GDA RGA o altre). Posizionamento catetere in sede idonea
- trasferimento a MN per studio scintigrafico MAA per shunt epato-polmonari
- ritorno in sala angio per
  - Se shunt + → rimozione catetere o terapia intravascolare alternativa
  - Se shunt - → rimozione catetere

eligibilità

Ordine Microsfere Ittrio
ed appuntamento per trattamento a 15-30 gg.

Arrivo Ittrio

Calibrazione Ittrio e dosimetria

**FASE 2:**
**ESECUZIONE**

Studio angiografico e posizionamento catetere→ TRATTAMENTO Y90

Scintigrafia di controllo dopo l'infusione

degenza 1-2 gg presso Ter. Radiometabolica
e poi Reparto di provenienza

Follow-up TC /PET , laboratorio

# Effetti Collaterali

- **Molto precoci (ore):** dolore, nausea

  40-60%, a causa dell'ischemia?

- **Precoci (giorni):** dolore, nausea, alterata funzionalità epatica

  estremamente raro

- **Tardivi (settimane):** affaticamento, anoressia

  frequenti, ma blandi

# **SIRT** (Selective internal radiation therapy): **Complicanze**

- **pancitopenia da soppressione midollare** (diffusione delle microsfere nel circolo sistemico)
- **polmonite attinica** (eccessivo shunting epato-polmonare)
- **colecistite** (passaggio di microsfere nell'arteria cistica)
- **ulcera gastrica e duodenale**, per passaggio delle microsfere attraverso ramificazioni arteriose viscerali extraepatiche ed impianto delle stesse nella parete di questi organi.
- **epatopatia** ed insufficienza epatica da radiazioni
- **…. Costi!**

Br J Cancer. 2010 Jul 27;103(3):324-31. doi: 10.1038/sj.bjc.6605770. Epub 2010 Jul 13.

# Multi-centre phase II clinical trial of yttrium-90 resin microspheres alone in unresectable, chemotherapy refractory colorectal liver metastases.

Cosimelli M, Golfieri R, Cagol PP, Carpanese L, Sciuto R, Maini CL, Mancini R, Sperduti I, Pizzi G, Diodoro MG, Perrone M, Giampalma E, Angelelli B, Fiore F, Lastoria S, Bacchetti S, Gasperini D, Geatti O, Izzo F; Italian Society of Locoregional Therapies in Oncology (SITILO).

Regina Elena National Cancer Institute, Via Elio Chianesi, 53, 00144 Rome, Italy. mcosimelli@libero.it

## Abstract

**BACKGROUND:** This **multi-centre phase II clinical trial** is the first prospective evaluation of radioembolisation of patients with **colorectal liver metastases** (mCRC) who failed previous oxaliplatin- and irinotecan-based systemic **chemotherapy** regimens.

**METHODS:** Eligible patients had adequate hepatic, haemopoietic and renal function, and an absence of major hepatic vascular anomalies and hepato-pulmonary shunting. Gastroduodenal and right gastric arteries were embolised before hepatic arterial administration of **yttrium-90 resin microspheres** (median activity, 1.7 GBq; range, 0.9-2.2).

**RESULTS:** Of 50 eligible patients, 38 (76%) had received > or =4 lines of **chemotherapy**. Most presented with synchronous disease (72%), >4 hepatic **metastases** (58%), 25-50% replacement of total **liver** volume (60%) and bilateral spread (70%). Early and intermediate (>48 h) WHO G1-2 adverse events (mostly fever and pain) were observed in 16 and 22% of patients respectively. Two died due to renal failure at 40 days or **liver** failure at 60 days respectively. By intention-to-treat analysis using Response Evaluation Criteria in Solid Tumours, 1 patient (2%) had a complete response, 11 (22%) partial response, 12 (24%) stable disease, 22 (44%) progressive disease; 4 (8%) were non-evaluable. Median overall survival was 12.6 months (95% CI, 7.0-18.3); 2-year survival was 19.6%.

**CONCLUSION:** Radioembolisation produced meaningful response and disease stabilisation in patients with advanced, **unresectable** and chemorefractory mCRC.

PMID: 20628388 [PubMed - indexed for MEDLINE] PMCID: PMC2920024 **Free PMC Article**

Eur Radiol. 2013 Jan;23(1):182-9. doi: 10.1007/s00330-012-2556-5. Epub 2012 Jul 27.

# Radioembolisation with (90)Y-labelled resin microspheres in the treatment of liver metastasis from breast cancer.

Cianni R, Pelle G, Notarianni E, Saltarelli A, Rabuffi P, Bagni O, Filippi L, Cortesi E.

Department of Diagnostic and Interventional Radiology, Santa Maria Goretti Hospital, Via Guido Reni n. 1, 04100, Latina, Italy.

## Abstract

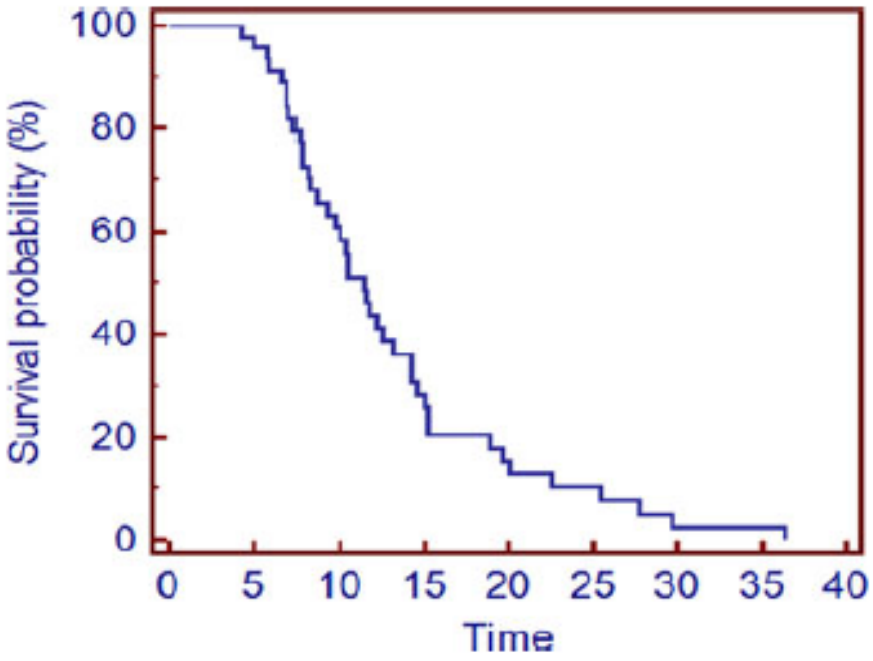
**OBJECTIVES:** Metastatic breast cancer is a heterogeneous disease, commonly affecting the liver. We report our experience with (90)Y radioembolisation (RE) and its effects on the survival of patients with treatment-refractory breast cancer liver metastases.

**METHODS:** A total of 77 female patients affected by breast cancer were accepted into our department for RE. Inclusion criteria were inoperable and chemotherapy-refractory hepatic metastases, acceptable performance status, sufficient residual liver, no significant hepato-pulmonary shunts. Patients were divided in two groups: group 1 (29 patients) included those with Eastern Cooperative Oncology Group (ECOG) score 0, liver involvement (0-25 %) and no extrahepatic disease (EHD); group 2 (23 patient) included patients with ECOG score 1-2, liver involvement (26-50 %) and evidence of EHD.

**RESULTS:** A total of 25 patients were considered ineligible. The median age of the remaining 52 patients was 57.5 years. The median overall survival was 11.5 months and better in those whose performance status and liver function were preserved (14.3 versus 8.2 months). According to Response Evaluation Criteria in Solid Tumor (RECIST), partial response (PR) was achieved in 29 patients (56 %), stable disease (SD) was achieved in a further 18 patients (35 %) and 5 patients showed progressive disease (PD) (10 %).

**DISCUSSION:** (90)Y RE is effective in the treatment of liver metastases from breast cancer. We demonstrated a relevant survival and encouragingly high response rate in patients with treatment-refractory disease.

PMID: **22836160** [PubMed - indexed for MEDLINE]




Kaplan–Meier curve depicts overall survival of all patients treated. Median survival for this cohort was 11.5 months calculated from the date of radioembolisation

Response of whole cohort according RECIST criteria

| Group | RECIST | | | |
|---|---|---|---|---|
| | CR | PR | SD | PD |
| 1 | 0 | 20 (54 %) | 15 (46 %) | 2 (5 %) |
| 2 | 0 | 9 (60 %) | 3 (20 %) | 3 (20 %) |

Surgery. 2013 Jun;153(6):801-10. doi: 10.1016/j.surg.2013.02.001.

# Right and extended-right hepatectomies for unilobar colorectal metastases: impact of portal vein embolization on long-term outcome and liver recurrence.

Ardito F, Vellone M, Barbaro B, Grande G, Clemente G, Giovannini I, Federico B, Bonomo L, Nuzzo G, Giuliante F.

Department of Surgery, Hepatobiliary Surgery Unit, Catholic University of the Sacred Heart, School of Medicine, Rome, Italy. francesco.ardito@rm.unicatt.it

## Abstract

**BACKGROUND:** **Portal vein embolization** (PVE) is an effective procedure to increase the future remnant **liver** (FRL) before major hepatectomy. A controversial issue is that PVE may stimulate tumor growth and can be associated with poor prognosis after **liver** resection for **colorectal liver metastases** (CRLM). The aim of this study was to evaluate the **impact** of PVE on **long-term** survival following major hepatectomy for CRLM.

**METHODS:** Between 1998 and 2010, 100 **right** and **extended-right hepatectomies** for **unilobar**, **right**-sided CRLM were performed. Of the group, 20 patients underwent preoperative PVE (group A). The control patients (group B; 20 patients) were selected by matching with the group A patients.

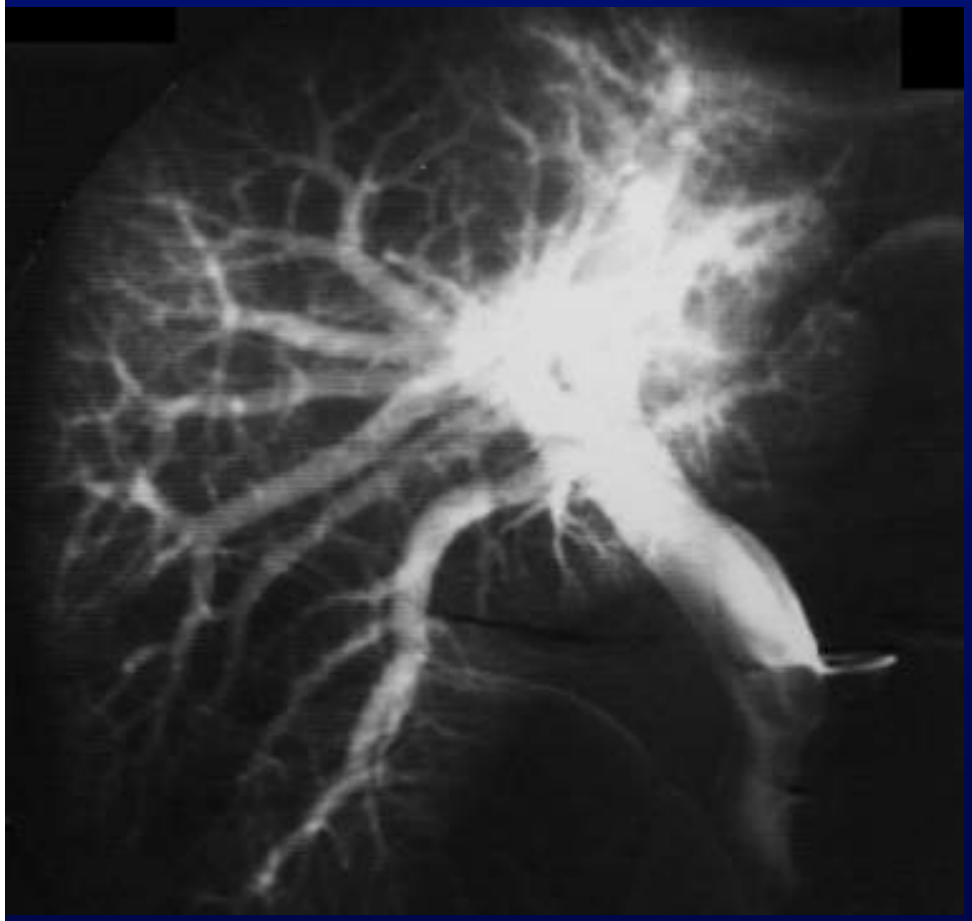
**RESULTS:** It was found that 25 patients (25/40; 62.5%) had developed tumor **recurrence**. The rate of global **recurrence** was not significantly different in groups A and B (65% vs 60%, respectively; P = .744). The specific overall intrahepatic **recurrence** rate was 42.5% (17 of 40 patients) and was not significantly different in groups A and B (45% vs 40%, respectively; P = .749). The 5-year overall and disease-free survival rates were similar in groups A and B (42.9% and 33.6% vs 42.1% and 27.7%, respectively). The 5-year specific **liver**-disease-free survival was 45.3% in group A and 53.5% in group B (P = .572). On multivariate analysis of all 100 **hepatectomies**, R1 resection (P = .013) was found to be the only independent predictor of **liver**-disease-free survival.

**CONCLUSION:** This study showed that PVE did not affect overall survival and specific **liver**-disease-free survival in patients undergoing **right** or **right**-extended hepatectomy for **unilobar**, **right**-sided CRLM.

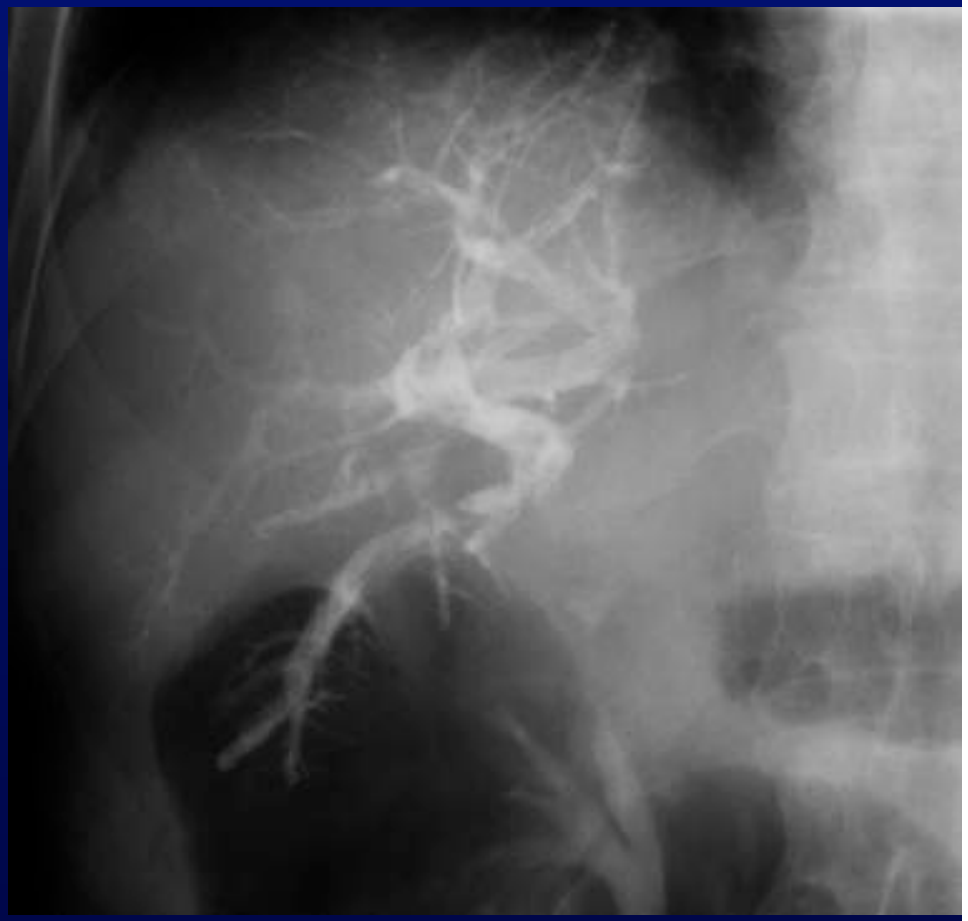


PMID: 23701876 [PubMed - in process]

# Embolizzazione portale



Portografia embolizzazione



Controllo post

Prevalence of portal vein embolization during colorectal liver metastasis resection.

| Authors, date | Interval | Total number of hepatectomies for CRLM | Major hepatectomies (*n*) | %[a] (*n*) Portal vein embolization | 5-year survival |
|---|---|---|---|---|---|
| Lindner et al., 2006 [22] | 1983–2004 | 243 | NA | NA (19) | Median: 32 months |
| Oussoultzoglou et al., 2006 [24] | 1995–2003 | 429 | 44 | 63% (28) | 44% |
| Mueller et al., 2008 [23] | 1995–2004 | 107 | 107 | 49.5% (53) | 44% |
| Covey et al., 2008 [21] | 1999–2004 | NA | 100 | NA (100) | NA |
| Pamecha et al., 2009 [25] | 1999–2005 | 168 | 109 | 33% (36) | 25% |
| Wicherts et al., 2010 [26] | 1990–2006 | 802 | 364 | 27% (99) | 21% |

NA: not available; CRLM: colorectal liver metastases.
[a] % of portal embolizations performed before major hepatectomy with intention to treat.

Complications after portal vein embolization during surgery for colorectal liver metastases.

| Authors, date | N Portal vein embolization | Morbidity (%) | Major complications after portal vein embolization |
|---|---|---|---|
| Pamecha et al., 2009 [25] | 36 | 6 | Main portal vein thrombosis (1) |
| Aussilhou et al., 2009 [67] | 28 | NA | Subcapsular hematoma (1) |
| Mueller et al., 2008 [23] | 53 | NA | Migration of embolization in the hepatic remnant (1) |
| Covey et al., 2008 [21] | 100 | NA | Asymptomatic arteriovenous fistula (1) |
| Lindner et al., 2006 [22] | 19 | NA | Biliary fistula (1) |
| Jaeck et al., 2004 [69] | 33 | 18 | Mesenterico-portal thrombosis (1), hematoma of the future remnant liver (1) |
| Azoulay et al., 2000 [51] | 30 | 3 | Hepatic necrosis (arterial injury) (1) |